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Editorial

Regional anesthesia and study of pain

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The Croatian Society of Regional Anaesthesia and analgesia is pleased to announce The 6th Croatian Congress of Regional Anaesthesia and analgesia with international participation in collaboration with the European Society of Regional Anaesthesia& Pain Therapy under auspices Croatian Academy Scientific and Arts in Zagreb, 12.–13. June 2015.

Tremendous changes have affected the practice of pain management and regional anesthesia, not just in relation to advances in pharmacologic and intervention aspects, but particularly in the manner by which these growing subspecialties are accepted in the delivery of health care. We have created this symposium to promote a better understanding of the pathophysiology of acute and chronic pain and to enhance the knowledge regarding various chronic neuropathic pain conditions as well as the novel state-of the-art interventional and non-interventional techniques in diagnosis and management of chronic pain, cancer pain and headache. We have assembled nationally and internationally renowned faculty to address current topics in acute, chronic, cancer pain management, and regional anesthesia.

Modern concept explicitly assumes that pain perception always has an underlying physical cause-injury, infection, or some disease process. Pain in the absence of such a cause is usually attributed to psychological illness or malingering. By recognizing the dominant role of the brain, which generates our subjective experiences and activates our defense systems, we are now able to appreciate the intimate relationship between pain and stress. These relationships among stress, gender, the immune system, and chronic pain syndromes reveal the need to study pain in a biological context far broader than a pain pathway.

The ultrasound and ultrasound guidance are the hottest fields in Regional Anaesthesia today. A lot of research still has to be done in order to prove that ultrasound really does improve our practice. Other hot topic is how Regional Anaesthesia can assist in improving the peri-operative outcome of patients. Not only the acute intra and immediately post-operation pain relief, but long term pain relief in addition to other parameters of outcome; inflammation, cancer recurrence, and speed of discharge from the hospital. Discusses how Regional Anaesthesia can be used as part of an integrated peri-operative approach to the patient. An additional topic is chronic pain management. This topic is an important aspect of Regional Anaesthesia and it is getting a lot of attention in Europe and the European commission as well.

We have a mission-all of us-to rectify the existing situation, for cancer pain as well as postsurgical pain, for pain in adults and in children, and for any kind of severe pain that can be helped by sensible administration of drugs and other pain therapies. In addition to educating one another in current pain research and therapy, as we do in journals and congresses, we must promote education on the management of pain for medical students and all health professionals. We must also teach patients to communicate better about their pain, and inform them that they have a right to freedom from pain, that each suffering human being deserves the best that the health professions have to offer.

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Leading article

Functional neuroanatomy of nociception and pain

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Abstract

Pain is a complex sensory state based on the integration of a variety of nociceptive inputs processed centrally through many parallel and overlapping neural systems. The traditional anatomical concept implies that nociceptive information is dominantly used to generate and regulate perception of pain through one major sensory pathway. It becomes recognized that experiencing the affective component of the pain is at least as important as perception. Also, nociceptive information is strongly influencing brain centers for regulating homeostasis. So, understanding neuroanatomical organization of central processing of nociceptive information is of great clinical importance. There is an attempt to simplify this complex set of interacting networks to a core set of brain regions or a generalizable pain signature. Herewith we wish to give a short overview of recent advances by presenting principles about neuroanatomical organization for processing various aspects of nociceptive inputs.

GENERAL NEUROANATOMICAL PRINCIPLES IN NOCICEPTIVE PROCESSING

Pain is the most distinctive of all the sensory modalities *(1)* but can be simply defined as the subjective experience associated with actual or potential tissue damage *(2–5).* It serves an important protective function and warns to avoid or treat injury. The perception of pain is subjective and can vary greatly among individuals. Moreover, in the same individual an identical sensory stimulus can elicit quite distinct conscious responses under different conditions. This includes also psychological conditions, such as fear or anxiety that can significantly influence the experience of pain. So, more than most sensory modalities, the perception of pain is influenced by emotional state and environmental contingency, is dependent on experience, and varies so markedly from person to person *(6–16),* and consequently remains notoriously difficult to treat .

Noxious stimuli, including tissue injury, activate nociceptors (from the Latin, noceo = to injure, hurt) which are present in peripheral structures and transmit information to the CNS: from the body to the spinal cord dorsal grey column, from the skin of the head to the spinal and principal trigeminal nucleus, and from the neck mucosa to the lower 2/3rd of solitary tract nucleus *(17–19).* To generate perception of pain the information should continue ultimately to the cerebral cortex. From anatomical point of view it should be noted that nociception refers to the process through which information about peripheral stimuli is transmitted by primary afferent nociceptors to the spinal cord, brainstem, thalamus, and subcortical structures. For the experience of pain, activity of thalamocortical networks that process the information conveyed by pathways of nociception is needed *(20–26)* (Figure 1).

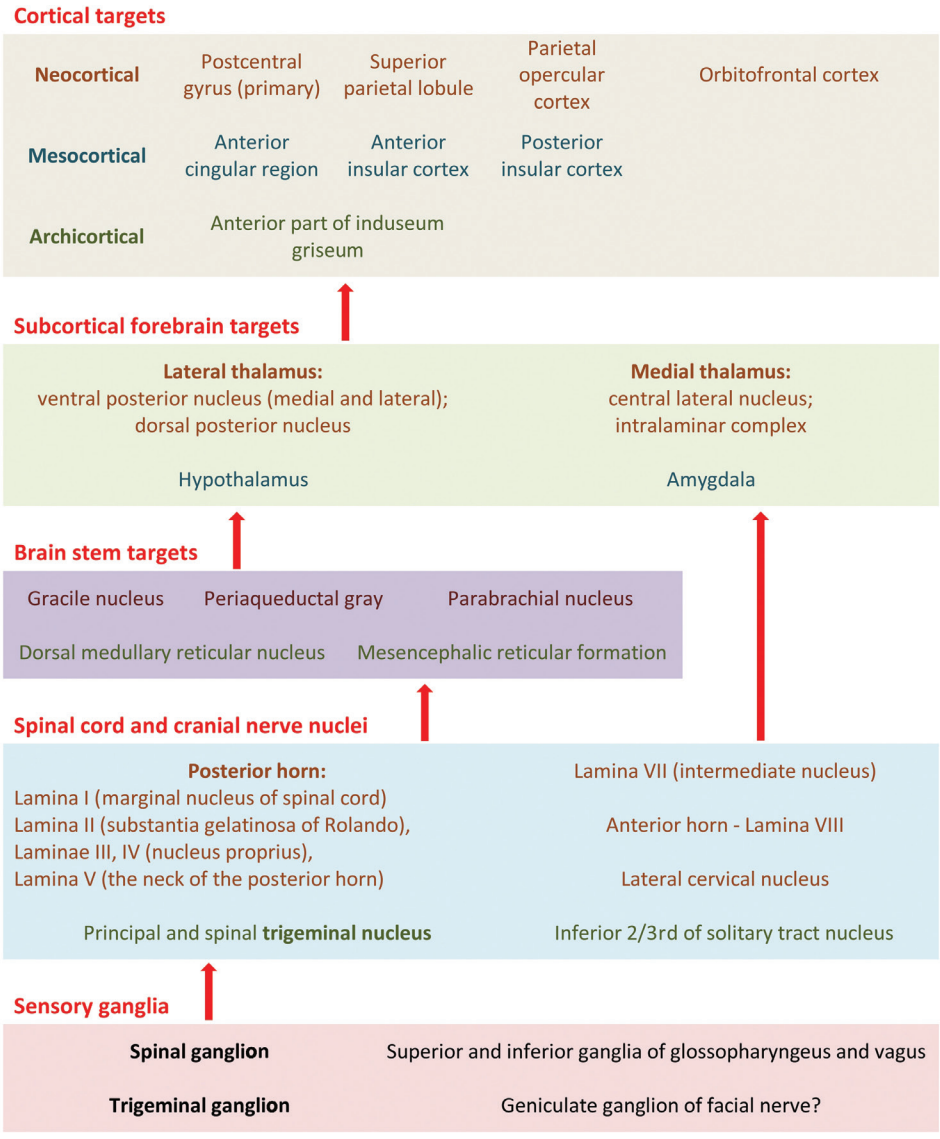

Figure 1. *Structures containing neurons processing nociception and pain.*

Pain sensation is not the direct expression of a sensory event. It has strong urgent and primitive quality with affective and emotional components *(7; 26–32),* and has also influence on homeostatic functioning *(33; 34).* By classical neuroanatomical description pain processing is dominantly related to spino- and trigemino-thalamic pathway *(17–19),* still this pathway is evolutionary newest in conducing nociceptive information *(35).* Pain is actually a complex sensory state that reflects the integration of many sensory signals and is the product of elaborate brain processing. Particularly complex processing is needed for experiencing the affective component of the pain and for the influencing on homeostasis. Numerous parallel and overlapping neural systems processing nociceptive information allow such a complex impact on the brain functioning *(22; 36–40).* Among the ascending pathways arising from the spinal cord and its trigeminal homologue are the spinothalamic and spinoreticulothalamic tracts, as well as the spinoparabrachial-amygdala pathway, which provides more direct access to limbic emotional circuits in the brain. There is an attempt to simplify this complex set of interacting networks to a core set of brain regions or a generalizable pain signature. Such approaches identify the following areas as key to experiencing pain: the thalamus, the posterior and anterior insula, the postcentral gyrus, the anterior cingulate cortex, and the periaqueductal gray matter. Functional specificity of this complex pattern is still unresolved.

Altogether, understanding neuroanatomical organization of central processing of nociceptive information is of great clinical importance *(41-45).* Herewith we wish to give a short overview of recent advances in under-

TABLE 1

Various classes of nociceptors associate with specific function in the detection of distinct pain submodalities.

Modality	Submodality	Nociceptors/fibers
Nociceptive Pain (somatic or visceral)	sharp cutting pain	mechanical nociceptors Aδ fibers
	dull burning pain	polymodal nociceptors C fibers
	deep aching pain from viscera	visceral nociceptors Aδ, C fibers
	burning pain	thermal-mechanical (hot) Aδ fibers
	freezing pain	thermal-mechanical (cold) C fibers
Non-Nociceptive Pain (neurophatic or symphatetic)	complex regional pain syndrome	no nociceptors
	post-herpetic neuralgia	
	phantom limb pain	
	anesthesia dolorosa	

standing neuroanatomical organization for various aspects of nociceptive processing and to relate neural structures and pathways to various submodalities of nociceptive processing.

MOLECULAR ANATOMY OF PERIPHERAL NOCICEPTIVE PROCESSING

Nociceptors, structures that respond selectively to stimuli that can damage tissue are widely distributed in the skin and deep tissues and include thermal, mechanical, and polymodal sensory receptors *(46-49)*. They respond directly to mechanical and thermal stimuli, and indirectly to other stimuli by means of chemicals released from cells in the traumatized tissue. Fourth class, so called "silent" nociceptors are found in the viscera. The nociceptors are free nerve endings of the peripheral axonal branches originating from primary sensory neurons. The cell bodies of nociceptors that convey information from the body are located in the dorsal root ganglia. Trigeminal ganglia and superior ganglia of glossopharyngeus and vagus contain somatic neurons processing nociceptive stimuli from skin, cranial periost and dura, the mucosa of eye, nasal sinuses, oral and nasal cavity and possibly part of tympanic tube and cavity. For the rest of tympanic tube and cavity, and the whole mucosa of pharynx and larynx primary visceral neurons are located in the inferior ganglia of glossopharyngeus and vagus *(17)*. The central branches of these primary neurons enter the central nervous system through spinal or cranial nerves where they make synaptic connections with a complex array of neurons that play different roles in nociceptive processing and pain. Trigeminal, glossopharyngeal and vagal nerve convey somatic information into the trigeminal nuclei, and visceral information into the nucleus of the solitary tract. The spinal nerve conveys nociceptive information from the body and viscera and terminates on neurons in the dorsal horn of the spinal cord. Afferent fibers innervating viscera project to the CNS through autonomic nerves; some spinal afferents travel along hypogastric, lumbar colonic and splanchnic nerves to terminate in thoracolumbar regions as part of sympathetic innervation, while vagal and pelvic afferents respectively terminate in the brainstem and lumbosacral cord and contribute to parasympathetic innervation. Thoracic branches of vagus also contain afferent fibers, but the nature to conduct pain information from thoracic and abdominal viscera is not clarified.

Based on the myelination of their afferent fibers nociceptors in the skin, muscle, joints, and visceral receptors fall into two broad classes *(2; 50-52)*. The first class are small diameter, thin myelinated Aδ fibers that innervate nociceptors producing short-latency pain described as sharp and pricking. The majority are mechanoreceptors because they are activated by sharp objects that penetrate, squeeze, or pinch the skin. In addition, many of these Aδ fibers also respond to noxious heat that can burn the skin. Electrophysiological studies have subdivided Aδ nociceptors into two main classes: type I and type II. Type I respond to both mechanical and chemical stimuli, but have relatively high heat thresholds (>50°C). These fibers mediate the first pain provoked by pinprick and other intense mechanical stimuli. Type II Aδ nociceptors have a much lower heat threshold, but a very high mechanical threshold; these fibers mediate the "first" acute pain response to noxious heat. The second class are nociceptors innervated by small diameter, unmyelinated C fibers producing diffusely distributed and poorly tolerated dull, burning pain. Under this heterogeneous class the most common type are polymodal nociceptors activated by a variety of noxious mechanical, thermal, and chemical stimuli, such as

pinch or puncture, noxious heat and cold, and irritant chemicals applied to the skin. Electrical stimulation of these fibers in humans evokes prolonged sensations of burning pain. Of particular interest are the heat responsive, but mechanically insensitive unmyelinated afferents (so-called silent nociceptors) that develop sensitivity when the chemical milieu of inflammation alters their properties *(53)*.

Visceral fibers can serve sensory function and evoke conscious sensations and also afferent function and regulate autonomic flow. Visceral sensory afferents are almost exclusively thinly myelinated Aδ-fibres and unmyelinated C-fibres. However, the distinction between nociceptive afferents and non-nociceptive afferents in the viscera is not clear. Nociceptors in the viscera that produce sensations of intense pain are activated by distension or swelling. Silent nociceptors found in the viscera are not normally activated by noxious stimulation. However, after tissue insult these nociceptors "wake up" in response to endogenous chemical mediators associated with tissue injury. Silent nociceptors are typically associated with increased spontaneous activity and responsiveness to noxious and even innocuous stimulus intensities. Their activation is thought to contribute to the development of secondary hyperalgesia and central sensitization, two prominent pain syndromes.

The membrane of the nociceptor contains protein complexes forming receptors and channels that transduce thermal, mechanical, or chemical energy of noxious stimuli into electrical impulses, which are propagated along the peripheral and central axon of the nociceptor into the central nervous system. Biochemical and molecular analysis of the nociceptor has identified multiple nociceptor subclasses, each expressing a distinctive repertoire of membrane ion channels, receptors and intracellular signaling proteins that are attractive targets for the development of drugs for therapeutic intervention in clinical pain conditions *(54-56)*. This includes voltage-gated sodium, potassium and calcium channels, leak channels, and ligand-gated channels such as acid-sensing ion channels and transient receptor potential (TRP) channels *(57)*. The role of transient receptor potential ion channels in thermal sensation was originally discovered by analyses of natural substances such as capsaicin and menthol that produce burning or cooling sensations when applied to the skin or injected subcutaneously. Capsaicin, the active ingredient in chili peppers, has been used extensively to activate nociceptive afferents that mediate sensations of burning pain *(58)*. The varieties of TRP channels in nociceptors underlie the perception of a wide range of temperatures from extreme cold to intense heat. Some classes of TRP receptors are activated by cold temperatures and inactivated by warming (TRPM8 and TRPA1receptors) while some types of TRP receptors are activated by warm or hot temperatures and inactivated by cooling (TRPV3, TRPV1, TRPV2 and TRPV4 receptors) *(59-61)*. A key role in the perception of pain in humans plays the voltage-gated sodium channel NaV1.7, found exclusively in the periphery and its mutation can lead to the inability to experience pain *(62)*. An ionotropic purinergic receptor, PTX3, that is activated by adenosine triphosphate (ATP) released from peripheral cells after tissue damage is also expressed by nociceptors *(63-65)*. In addition, nociceptors express members of the Mas-related G protein-coupled receptor (Mrg) family, which are activated by peptide ligands. They serve to sensitize nociceptors to other chemicals released in their local environment *(66-68)*.

Neuroanatomical and molecular characterization of nociceptors demonstrated their heterogeneity; various functionally and molecularly heterogeneous classes of nociceptors associate with specific function in the detection of distinct pain submodalities *(69)*.

MECHANISMS MODULATING NOCICEPTIVE PROCESSING

The proper function of the nociceptive system enables and enforces protective behavioral responses such as withdrawal or avoidance to acutely painful stimuli. In case of an injury the vulnerability of the affected tissue is going to increase *(70-75)*. The nociceptive system adapts to this enhanced vulnerability by locally lowering the nociceptive thresholds and by facilitation of nocifensive responses. The behavioral correlates of these adaptations are allodynia (condition in which non-noxious events are perceived as noxious) and hyperalgesia (mildly noxious events are perceived as highly noxious). However, hyperalgesia and allodynia may persist long after the initial cause for pain or may occur due to dysfunction of parts of the peripheral or central nervous system and become maladaptive rather than protective.

Two types of hyperalgesia, primary and secondary, are associated with different mechanisms. Primary hyperalgesia develops at the site of tissue injury associated with an increased sensitivity of the peripheral nerve fibers involved in pain. Secondary hyperalgesia develops in uninjured tissue surrounding the site of injury. This form of hyperalgesia is not caused by sensitization of nociceptive nerve endings but due to changes in the excitability of neurons in the central nervous system, including the spinal cord and supra-spinal sites in the brain. Recent evidence suggests, however, that altered processing in the central nervous system is equally important in the induction of primary hyperalgesia *(70)*.

Numerous mediators in the peripheral and central nervous systems contribute to the processes of sensitization. The sensitization of nociceptors is triggered by chemical mediators released from distinct cell types that accumulate at the site of tissue injury and act together to decrease the threshold of nociceptor activation, such as histamine, anandamide, acetylcholine, serotonin, norepinephrine,

prostaglandin, bradykinin, substance P and calcitonin gene-related peptide. Central sensitization is a considerably more complicated process that can result from increased release of excitatory neurotransmitter (e.g., glutamate, substance P) and/or enhanced synaptic efficacy. These changes relate to several cellular mechanisms (a) presynaptic changes, (b) postsynaptic changes, (c) interneuron changes, (d) changes in descending modulation, and (e) immune/microglial mechanisms *(76; 77)*.

The understanding of pain mechanisms and pain control has focused on the properties of primary afferent and dorsal horn nociceptive neurons and ascending pathways. However, there is an active regulation of sensory transmission at the level of the dorsal horn by descending projections arising from a number of brain sites *(78-89)*. Descending control plays a critical role in determining the experience of pain and can be facilitatory as well as inhibitory. The balance between inhibition and facilitation is dynamic, and can be altered in different behavioral, emotional and pathological states. For example, intense stress and fear are associated with decreased responsiveness to noxious stimuli that reflects a shift towards descending inhibition. By contrast, inflammation and nerve injury, sickness, and chronic opioid administration are associated with hyperalgesia that in part reflects a shift towards descending facilitation. There is much evidence to suggest that descending facilitation of spinal nociception is a major contributor to central sensitization and the development of secondary hyperalgesia.

Descending control arises from a number of supraspinal sites, including the midline periaqueductal gray-rostral ventromedial medulla (PAG-RVM) system, and the more lateral and caudal dorsal reticular nucleus (DRt) and ventrolateral medulla (VLM). Serotonergic neurons settled in the raphe nuclei and neorepinephrine neurons settled in the locus coerlues play the major role in descending control. Inhibitory control from the PAG-RVM system preferentially suppresses nociceptive inputs mediated by C-fibers, preserving sensory-discriminative information conveyed by more rapidly conducting A-fibers. Analysis of the circuitry within the RVM reveals that the neural basis for bidirectional control from the midline system is two populations of neurons, ON-cells and OFF-cells that are differentially recruited by higher structures important in fear, illness and psychological stress to enhance or inhibit pain.

FUNCTIONAL NEUROANATOMY OF CENTRAL NOCICEPTIVE PROCESSING

The pain-related circuitry extends over both the cognitive and the emotional-motivational domains of the brain. It includes the spinothalamic component of the anterolateral fasciculus, the trigeminothalamic tract and pathways that connect the spinal cord and the sensory nuclei of the trigeminal nerve with the brain stem, the hypothalamus and the basal forebrain *(17)*.

The central branches of primary neurons enter the central nervous system and make synaptic connections with a complex array of neurons. This triggers the release of neurotransmitters such as glutamate and substance P, which activate second-order neurons that project to the brain. The spinal gray dorsal horn-column (and its equivalent, the caudal part of trigeminal nerve nucleus) constitutes one of the main relay stations for primary afferents of the dorsal roots.

Besides nociceptive-specific neurons, the spinal dorsal horn (especially deeper laminae) also contains wide dynamic range (WDR) neurons that respond to both innocuous and noxious stimuli. After entering the spinal cord (through lateral division of peripheral nerve) small myelinated Aδ and unmyelinated C fibers terminate in the dorsal horn. The spinal gray matter in the dorsal horn is divided into six layers of cells *(90-93)*. Nociception specific neurons in the lamina I respond selectively to noxious inputs from Aδ or C fibers and project to higher brain structures. Other classes of lamina I responed to both innocuous and noxious mechanical stimulation and thus are termed wide-dynamic-range neurons. Neurons in laminae II and III are interneurons that receive inputs from Aδ and C fibers, and make excitatory or inhibitory connections to neurons in lamina I, IV, and V that project to higher brain centers. Wide-dynamic-range neurons in lamina V typically respond to a wide variety of noxious stimuli and project to the brain stem and thalamus. Neurons in lamina V also receive input from nociceptors in visceral tissues.

Many neurons located in laminae VII and VIII, building the intermediate grey and deep part of ventral gray column, have complex response properties to noxious stimuli because the inputs from nociceptors to these neurons are conveyed through many intervening synapses. Whereas most dorsal horn neurons receive unilateral input, neurons in lamina VII often respond to stimulation of both side of the body and therefore contribute to the diffuse quality of many pain conditions. Visceral C fibers terminate ipsilaterally in laminae I, II, V, and X and also in lamina V and X of the contralateral gray matter.

Finally, fibers from lamina I and the nucleus of the solitary tract convey information about impending and actual tissue damage, and a wide range of visceral stimuli; the responses of neurons in lamina V correlate closely with reports of pain intensity, while the lamina VII plays a significant role in emotional responses to sensory stimuli.

Five major ascending pathways contribute to the central processing of nociceptive information: the spinothalamic, spinoreticular, spinomesencephalic, cervicothalamic, and spinohypothalamic tracts.

From neurons in laminae I, V, and VII, the main targets of the small-diameter fibers with sensory information destined for conscious perception, originates the spinothalamic tract that is the principal pathway transmitting noxious, thermal, and visceral information to the thalamus and cerebral cortex *(94).* The axons of most neurons in lamina I cross the midline, just ventral to the central canal, and ascend in the contralateral lateral spinothalamic tract located in the lateral funiculus. Axons of lamina V neurons cross the spinal cord and ascend in the contralateral ventral spinothalamic tract. Axons from the caudal part of spinal trigeminal nucleus form tractus trigeminothalamicus lateralis that crosses the midline and joins the spinothalamic tract. As a result of the decussation of spinothalamic fibers in the spinal cord, noxious information from each dermatome is transmitted contralaterally in the anterolateral column. The importance in pain processing through the sphinothalamic tract is demonstrated by experimental and clinical evidence. Electrical stimulation is sufficient to elicit the sensation of pain and anterolateral cordotomy results in a marked reduction in pain sensation on the side of the body contralateral to that of the lesion. As mentioned, information carried by small-diameter sensory fibers also reaches the cerebral cortex through several polysynaptic routes other than the spinothalamic tract *(38-40; 95).* Although many of these pathways originate from neurons in lamina I and V, they arise from a different group of neurons and project to brain stem nuclei which in turn project to the thalamus and to other sites, such as the hypothalamus and amygdala. Neurons that project to sites other than the thalamus are involved in homeostatic control, by regulating endocrine release and autonomic activity. The spinoreticular tract ascends in the anterolateral quadrant of the spinal cord and terminates in both the reticular formation and the thalamus. It contains the axons of projection neurons in laminae VII and VIII and do not cross the midline. The spinomesencephalic (spinoparabrachial) tract projects in the anterolateral quadrant of the spinal cord to the mesencephalic reticular formation and periaqueductal gray matter. It contains the axons of projection neurons in laminae I and V. Information transmitted along this tract are thought to contribute to the affective component of pain. They also course through the dorsal part of the lateral funiculus and project to the parabrachial nucleus. Neurons of the parabrachial nucleus project to the amygdala, a key nucleus of the limbic system that regulates emotional states. The spinohypothalamic tract projects to hypothalamic nuclei that serve as autonomic control centers involved in the regulation of the neuroendocrine and cardiovascular responses that accompany pain syndromes. It contains the axons of neurons in laminae I, V, and VIII. The cervicothalamic tract runs in the lateral white matter of the upper two cervical segments of the spinal cord and contains the axons of neurons of the lateral cervical nucleus, which receives input from neurons in laminae III and IV of the dorsal horn. Most axons in the cervicothalamic tract cross the midline and ascend in the medial lemniscus of the brain stem, terminating in midbrain nuclei and in the ventroposterior nuclei of the thalamus. The signals from nociceptors in the pelvic and abdominal viscera are relayed through other neurons in laminae III and IV of the sacral and midthoracic spinal cord which project axon through the most medial part of the white dorsal column terminating in the gracile nucleus.

The thalamus represents a key integrative structure for the processing of pain and thus contains several relay nuclei that participate in the central processing of nociceptive information.

The lateral nuclear group comprises the ventroposterior medial nucleus, the ventroposterior lateral nucleus, and the dorsal posterior nucleus that receive inputs from nociception-specific and wide-dynamic-range neurons in laminae I and V of the dorsal horn through the spinothalamic tract. The lateral thalamus is thought to be concerned with the processing of information about the precise location of an injury, information usually conveyed to consciousness as acute pain. The medial nuclear group of the thalamus comprises the central lateral nucleus of the thalamus and the intralaminar complex and receives major input from neurons in laminae VII and VIII of the spinal cord. Many neurons in the medial thalamus respond optimally to noxious stimuli and project widely to the basal ganglia and different cortical areas. The pathway to the medial thalamus was the first spinothalamic projection evident in the evolution of mammals and is therefore known as the paleospinothalamic tract. It is also sometimes referred to as the spinoreticulothalamic tract because it includes indirect connections through the reticular formation of the brain stem. The projection from the lateral thalamus to the ventroposterior nuclei is most developed in primates, and is termed the neospinothalamic tract.

Regarding cortical processing it should be emphasized that pain is a complex perception that involves many areas. Spatial, temporal and intensity aspects of pain perception are processed in the primary and secondary somatosensory cortex (S1 and S2, respectively). The anterior cingulate cortex and insular cortex are involved in processing emotional states associated with pain, while the dorsal posterior insula contributes to the autonomic component of pain responses. Moreover, the prefrontal cortex with corresponding mediodorsal thalamic nucleus and premotor areas in connection with cerebellum are also commonly activated by painful stimulation.

FUNCTIONAL NEUROANATOMY OF PAIN SUBMODALITIES

The sense of pain includes a response to external events that damage or harm the body and therefore belongs to

extroceptive sensation. Although the sense of the function of the major organ systems of the body and its internal state (interoception) do not become conscious sensation, abnormal function in major organ systems resulting from disease or trauma can evoke conscious sensations of pain.

When pain is experienced it can be acute, persistent or chronic *(76).* Persistent pain characterizes many clinical conditions and is usually the major reason why patients seek medical attention. In contrast, chronic pain does not serve a useful biological function; it only makes patients miserable *(7; 31; 32; 96-101).* Persistent pain can be subdivided into two broad classes, nociceptive and neuropathic (Table 1). Nociceptive pains result from the direct activation of nociceptors in the skin or soft tissue in response to tissue injury and usually arise from accompanying inflammation. Sprains and strains produce mild forms of nociceptive pain, whereas arthritis or a tumor that invades soft tissue produces a much more severe nociceptive pain. Pain may also result from injury to sensory fibers or from damage to the central nervous system. These types of pain are designated as non-nociceptive or neuropathic pain *(77; 102-105).* Neuropathic pains include the syndromes of reflex sympathetic dystrophy, also called complex regional pain syndrome, and post-herpetic neuralgia, the severe pain experienced by patients after a bout of shingles. Other neuropathic pains include phantom limb pain *(106-109),* the pain that occurs after limb amputation. In some instances pain can even occur without a peripheral stimulus, a phenomenon termed anesthesia dolorosa. This syndrome can be triggered following attempts to block chronic pain, for example after therapeutic transection of sensory afferent fibers in the dorsal roots.

Sharp, pricking pain is produced by nociceptors innervated by Aδ fibers and activated by sharp objects that penetrate, squeeze, or pinch the skin (mechanical nociceptors). Dull, burning pain that is diffusely localized and poorly tolerated is produced by nociceptors innervated by C fiber (polymodal nociceptors). When a stone hits your elbow, you initially feel a sharp, fast, momentary pain, called first pain and conveyed by Aδ fibers followed by a more prolonged aching and sometimes burning pain ("second pain") which is transmitted by the C fibers.

There is a clear demarcation between the perception of innocuous warmth and noxious heat. This enables us to avoid temperatures capable of causing tissue damage. If skin temperature changes slowly, we are unaware of changes in the range 31° to 36°C. Below 31°C the sensation progresses from cool to cold and finally, beginning at 10° to 15°C, to pain. Above 36°C the sensation progresses from warm to hot and then, beginning at 45°C, to pain. The freezing pain is produced by cold nociceptors innervated by C fibers, while the burning pain is produced by heat nociceptors innervated by Aδ fibers. Thermal stimuli activate specific classes of TRP ion channels in the membrane *(60).* Two classes of TRP receptors are activated by cold temperatures and inactivated by warming; TRPM8 receptors respond to temperatures below 25°C (such temperatures are perceived as cool or cold), while TRPA1 receptors have thresholds below 17°C (this range is described as cold or frigid). Four types of TRP receptors are activated by warm or hot temperatures and inactivated by cooling; TRPV3 receptors are expressed in warm type fibers and they respond to warming of the skin above 35°C (generate sensations ranging from warm to hot). TRPV1 and TRPV2 receptors are expressed in heat nociceptors and respond to temperatures exceeding 45°C (mediate sensations of burning pain). TRPV4 receptors are activated by temperatures above 27°C and respond to normal skin temperatures.

Visceral pain (deep aching pain) is sensations of intense, diffuse, often poorly localized pain. Diffuse nature and difficulty in locating visceral pain is due to a low density of visceral sensory innervation and extensive spinal distribution of visceral C fibers. Visceral pain is often associated with marked autonomic phenomena: nausea, gastrointestinal disturbances, pallor, profuse sweating, and changes in blood pressure, heart rate and body temperature. In addition, visceral pain frequently produces referred pain, a condition in which pain from injury to a visceral tissue is perceived as originating from a region of the body surface. Referred pain is sharper, better localized and less likely to be accompanied by autonomic signs, and therefore difficult to differentiate from pain of somatic origin. Convergence of visceral and somatic afferent fibers may account for referred pain phenomenon. Nociceptive afferent fibers from the viscera and fibers from specific areas of the skin converge on the same projection neurons in the dorsal horn (lamina V neurons). Thus, a signal from this neuron does not inform higher brain centers about the source of the input and the brain incorrectly attributes the pain to the skin. Another anatomical explanation for instances of referred pain is that the axons of nociceptive sensory neurons branch in the periphery, innervating both skin and visceral targets *(110; 111).*

There is one unpleasant sensation showing considerable apparent overlap in the neuronal cells and circuits that transmit pain, the itch. It is characterized by a strong innate urge to scratch and is confined to the skin, the ocular conjunctiva, and the mucosa. Itch was considered to be related to pain, because painful stimuli such as scratching inhibits while some analgesics (e.g. opioids) can cause itch. In addition, some itch-causing compounds (pruritogens) induce inflammatory pain, and under certain circumstances some pain-causing compounds (algogens) induce itch. Finally, there is a broad overlap between relevant mediator systems in pain and itch. Parallels between pain and itch processing are even more evident in the pattern of central sensitization. Touch- and pin prick-induced pain (allodynia and punctate hyperalgesia) correlate to touch- and pin prick induced itch (alloknesis and punctate hyperknesis). However, recent discoveries about

molecular and cellular basis of itch cover diverse aspects of itch sensation, from the identification of new receptors to the characterization of spinal cord itch circuits. These studies demonstrate that itch sensory signals are clearly demarcated from input of other somatosensory modalities (pain, touch, temperature) that is achieved by the expression of dedicated receptors and transmitters in a select population of sensory neurons which detect pruritogens. Also, itch specificity is maintained in a spinal cord circuit by the utilization of specific neurotransmitters and cognate receptors to convey input along a distinct cellular pathway *(112-116).*

Recent advances in molecular and anatomical processing of pain: clinical implications

Impressive insights into the molecular mechanisms of peripheral pain transduction has been recently developed opening the way for more effective pain therapies. Human genetics and molecular biology have revealed specific channels expressed selectively by nociceptive sensory neurons, such as TRP and Na channels, what has led to the development of many small-molecule channel antagonists some of which may prove to be effective as selective peripheral analgesics. The use of transcutaneous and dorsal-column electrical stimulation in the control of certain types of peripheral pain was encouraged by the finding that the balance of activity in small- and large-diameter sensory fibers modulates the perception of pain. Also, an observation that stimulation of specific sites in the brain stem produces deep analgesia has encouraged efforts to control pain by activating endogenous modulatory systems. In certain clinical conditions intrathecal and epidural administration of opiates induces a potent analgesia. However, understanding of the organization of central pain circuits under normal and pathological conditions remains relatively incomplete and thereby for most central pain syndromes there are still no effective pain therapies. It is expected that the future progress in pain therapy will depend on the research finding about brain circuits that transmit nociceptive signals *(2; 117-120).*

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What is new in education and teaching in regional anaesthesia?

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INTRODUCTION

Training of some procedures on live patients is no longer ethically justified or acceptable to the patient. Patients expect that health professionals have fully mastered a procedure before using it on them. Procedures performed on a patient simulator can be interrupted, improved and repeated and, unlike in real life, no harm is done when a mistake is made *(1)*.

SIMULATION TEACHING AND LEARNING IN REGIONAL ANAESTHESIA

Various types of simulators are used to train and assess different levels of learners. These include human cadaver, mannequin simulators or animal models, computer-based simulation, haptic and or virtual simulation, as well as simulation using standardized patients (2). One of the prerequisites for physician, who wish to take the European Diploma in Regional Anaesthesia and Pain therapy (EDRA) Part I, is to attend a minimum of 1 ESRA workshop or CME/CDP approved workshop. The following are considered ESRA workshops: ESRA Congress WS, ESRA Cadaver WS in Innsbruck or Ljubljana, ESRA Winter Week in Grindelwald (http://esraeurope.org/education/esra-diploma/). Evaluation of cadaver workshops for education in regional anaesthesia demonstrated that the practice of peripheral nerve blocks on cadavers represents the most important part of the course *(3)*.

Although cadavers are used to teach anatomy and technical skills for regional anaesthesia, utilisation of ultrasound-guided simulator for technical skill training has become a trend in recent years. The observation of novice's behaviour, associated with learning ultrasound-guided peripheral regional anaesthesia, demonstrated that two main mistakes wre failure to visualize the needle before advancement and unintentional probe movement. They concluded that this technical part of block can be improved with preclinical simulation training *(4)*. Recent study also showed that simulation would still be applicable to all peripheral nerve blocks with respect to localization of target and placement of needle to the target *(5)*. There is commercially available ultrasound training block model for acquisition and interpretation of sonographic images of nerves and vessels and for developing the psychomotor skills of guiding needles to simulated nerves and vessels. Sonoanatomically based part-task simulators for learning ultrasound guided regional anaesthesia are also commercially available: an upper body torso manikin for learning interscalene and infraclavicular nerve blocks, a femoral model for learning femoral nerve blocks, and leg model for learning sciatic nerve blocks in

the subgluteal and popliteal areas (Blue Phantom Ultrasound Training Models). These simulators were developed to anatomically mimic both surface anatomy and the sonoanatomy present on ultrasound visualization *(6)*. Epidural and spinal anaesthesia simulators consist of a torso with synthetic spinal column that includes a ligamentum flavum and a spinal cord within a fluid-filled thecal sac. These trainers can reasonably recreate the touch, feel and consistency of a normal human back and the structures involved in neuroaxial regional techniques. Some models allow ultrasound imaging *(7)*. Recommendations for education and training in ultrasound-guided regional anaesthesia by the American Society of Regional Anaesthesia and Pain Medicine as well as the European Society of Regional Anaesthesia and Pain Therapy suggest one method for education is to practice needle insertion techniques using simulators and phantoms *(8)*. Increasingly sophisticated regional anaesthesia simulators continue to be developed although the contribution for such models to attainment regional anaesthesia skills remains to be seen *(7)*.

For teaching and practicing how to manage critical events associated with peripheral neuroaxial and nerve blocks such as phrenic nerve paralysis with respiratory failure, stellate ganglion block with Horner' s syndrome, tension pneumothorax with cardiovascular collapse, recurrent laryngeal nerve block with hoarseness, central neuroaxial blockade with cardiovascular and respiratory collapse and intravascular injection of local anaesthetic, can be simulated with the high-tech computer controlled manikin. That manikin is specifically designed for training in anaesthesia, respiratory and critical care provides respiratory gas exchange, anaesthesia delivery and patient monitoring with real physiological clinical monitoring. The trainee can: "talk" to the mannequin and get answers from the operator through a speaker in the mannequin's head. The trainee can check the pupils, which react to light, feel arterial pulses, listen to cardiac and lung sounds, and collect information on heart rate, blood pressure, respiratory rate and oxygen saturation. Medications and fluids can be administered to the simulator, which responds appropriately based on an interaction between the mannequin's current underlying physiology and the dose, pharmacokinetics and pharmacodynamics of the medication. In addition, a number of procedures such as airway management, cricothyroideotomy and chest drain insertion can be performed on the mannequin (HPS Human Patient Simulator, CEA Healthcare).

Figure 1. *Trainee is performing spinal anaesthesia on the part-task trainer. Medical Simulation Unit, University Medical Center Ljubljana.*

Figure 2. *Operation theatre in Medical Simulation Unit, University Medical Center Ljubljana.*

In the University Medical Centre Ljubljana, Medical Simulation Unit was officially opened on 29th June 2011. It is multidisciplinary skills centre which can deliver a diverse number of training activities to national and international medical practitioners and healthcare workers. The centre has one operating theatre with associated control room, one intensive care unit with associated control room, two briefing – debriefing rooms with e-learning pods, storing space, wardrobe and external training area. Out trainees have the opportunity to train the regional anaesthesia using part-task trainers and management of critical events associated with regional anaesthesia with high-tech computer controlled manikin.

CONCLUSION

Simulation based clinical training is a supplement, not a replacement for traditional training and maintenance of competence. Learning on mistakes is done with no harm for the patients. It has been identified that simulation based clinical training can shorten the learning curve, permit manual skills development before patient

exposure, improve performance under stress, improve team work and optimise communication. It is more than just a novel education strategy. Over the next decade it should mature into a key tool for error mitigation *(9)*.

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Perioperative analgesia for thoracic surgery

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Abstract

Pain after thoracic surgery can be severe and it contribute to perioperative morbidity and mortality. After thoracotomy, pain can be result of many factors, including the skin incision and deeper tissue injuries and trauma, thoracostomy tubes, costovertebral joint disruption, rib and sternum fractures. The role of well planned pain management has been crucial in decreasing morbidity after major thoracic for lung resection. Many methods of analgesia have been described to surgery the posttoracotomy pain and prevent the development of the postthoracotomy pain syndrome: modification of surgical technique, intercostal nerve block, intrapleural analgesia, lumbar and thoracic epidural, paravertebral block, intravenous narcotics together or without the use of nonsteroidal antiinflammatory drugs. Multimodal pain management strategies can improve postoperative pain management while contributing other outcome benefits to our high-risk patient population.

INTRODUCTION

The alleviation of postoperative pain is primary provided for humanitarian reasons, but also to reduce nociception-induced responses, which may adversely influence organ functioning and contribute to morbidity. Major surgery elicits profounding physiologoical changes including hormonal, metabolic and immunological responses. Surgical injury, trauma and infection of a tissue induce an acute inflammatory reaction with excessive mediator release. The response to injury is initiated by somatic and autonomic nerve impulses and the release of cytokines and other inflammatotory mediators *(1, 2).*

A local inflammatory response always occurs in relation to surgical trauma. Severe injury or multiple trauma evoke a systemic inflammatory response. This systemic inflammatory response to major injury is caused by hormonal, metabolic and immunological mediators, and is associated with a haemodynamic response *(3).* Surgical trauma is also associated with ischemia, ischemia/reperfusion (I/R) injury, hypovolemia and the immunological reactions secondary to blood transfusion *(3).* The systemic inflammatory response is required for tissue repair and has evolved in all mammals to optimise the healing potential of an organism. In uncomplicated surgical patients the systemic inflammatory response is temporary, predictable and well balanced between pro- and anti-inflammatory mediators *(3).* If the patient is exposed to severe major surgical trauma an initial exaggerated proinflammatory response may be observed *(3).*

After a major surgery a pulsatile release of stress hormons occures. The net effect of the neuroendocrine response to surgery is an increased secretion of the catabolic hormones, with increased catabolism. Hormonal, metabolic and immune stress response can result in increased

perioperative morbidity and mortality. Knowledge of the normal inflammatory and hormonal response to trauma makes it possible for the anaesthetist or surgeon to react if an abnormal response is observed. Undesirable aspects of the surgery can be decreased by the use of appropriate surgical (minimal invasive surgery) and anaesthesiological techniques (use of volatile anaesthetics, protective ventilation, appropriate fluid resusscitation,…). It can be minimised also by certain analgesic techniques *(1, 2, 3)*.

In the following discussion, we briefly review the current literature surrounding pain management after thoracic surgical procedures and propose an approach.

MECHANISM OF PAIN

Pain can be defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, as described in terms of such damage. Visceral pain is the most common form of pain produced by surgical injury *(2)*. Local tissue damage results in inflammation and propagation of stimuli to the central nervous system. Nocioceptors may be associated with small myelinated A delta group fibres or unmyelinated C fibers afferents. Painful stimuli ascend through the the spinal cord in to the spinothalamic trackts and are modulated by excitatory (N-methyl-Daspartate [NMDA]) and inhibitory (opiate) pathways *(4)*. Clinical and laboratory observations suggest that pain can result in hyperexcitability in the spinal cord, resulting in increasing levels of perceived pain. This process, also known as central sensitization or "wind-up," involves conduction of impulses along afferent C-fibers, and release of excitatory neurotransmitters such as glutamate and aspartate through the NMDA receptor *(4)*. In the perception of the pain stimuli also psychological factors play an important role *(2)*.

The existence of chronic pain after surgery is well known and described through out the years *(5)*. To evaluate pain after surgery following criteria must be met: the development of pain after surgical procedure; pain, which persist for at least 2 months; malignant lesions and/or inflammation must be excluded and no previous chronic pain syndrome encountered *(5, 6)*.

PAIN MANAGEMENT FOR THORACOTOMY

Pain after thoracic surgery can be severe and it contribute to perioperative morbidity and mortality.

Beside acute pain this patients also incur a significant risk of chronic pain. Although there are guidelines for postoperative pain management in these patients, there is no widespread surgical or anesthetic "best practice" *(7)*.

After thoracotomy, pain can be result of many factors, including the skin incision and deeper tissue injuries and trauma, thoracostomy tubes, costovertebral joint disruption, and rarely rib- or sternum- fractures. Pain from a thoracotomy incision is considered to be severe and intense as a consequence of tissue damage to the ribs, muscles, and peripheral nerves *(4, 7)*

The typical patient undergoing thoracic surgery has little reserve to tolerate adverse effects from the complications of poor pain management. Common comorbid conditions beyond lung disease include advanced age, heart disease, renal dysfunction, and obesity *(4, 7)*. Patients undergoing thoracotomy are often deconditioned secondary to their poor pulmonary function or treatment of their respiratory condition, including chemotherapy, radiation, immune compromise, malnutrition, and related anemia *(7)*.

The role of well-planned pain management has been crucial in decreasing morbidity after major thoracic surgery for lung resection. Pain is a key component in the alteration of lung function after thoracic surgery, highlighting the importance of providing effective postoperative analgesia to reduce pulmonary complications and attenuate the stress response *(7)*. Various analgesic techniques have been developed to treat postoperative thoracotomy pain; however, acute and chronic pain conditions associated with thoracotomy continue to present a problem to clinicians *(4, 7)*.

Strategies have been created to minimize pain and create a "best practice" for patients undergoing thoracotomy. A primary surgical shift in using minimally invasive, video-assisted thorascopic surgery (VATS) whenever possible has been supported in part by studies reporting reduced incisional pain in the acute period when compared to thoracotomy *(8)*. In the cardiac surgery realm, when compared to sternotomy, minimally invasive port-access cardiac surgery has not resulted in less pain. Unfortunately, patients undergoing thoracotomy and VATS alike continue to experience chronic pain at an alarmingly high incidence, 4–8 with about one third developing a neuropathic component *(7, 9)*.

Uncontrolled acute perioperative pain and related surgical stress responses are associated with higher perioperative morbidity, longer hospitalization, lower patient satisfaction, and higher costs(10). Unalleviated pain in the perioperative period also predicts the development of chronic pain- postthoracotomy pain syndrome *(7)*.

Postthoracotomy pain syndrome is defined as pain that recurs or persists along a thoracotomy incision at least two months following the surgical procedure. Chronic pain after thoracic surgery has the prevalence of 9–80% for thoracotomy and 5–33% for video-assisted thoracoscopic surgery *(11)*. Such a difference in the prevalence of postthoracotomy pain can be attributed to several factors, including the intraoperative technique, anaesthesia and postoperative analgesia *(11)*. The exact cause of the development of post-thoracotomy pain syndrome has not been

established, possible causes include the damage of intercostal nerve (rib retraction, troacar insertion, suture placement), type of incision, personality traits (preoperative anxiety) and pain due to extensive rib retraction (disarticulation of costochondral/costovertebral junctions, injuries to the muscles) *(12, 13)*. Some authors also include suboptimal management of acute post-thoracotomy pain as one of the major causes in developement of this syndrome. The patient, suffering from post-thoracotomy pain syndrome typically describes his pain as stabbing or burning in nature, dysaesthesias are almost obligate. Pain worsens on deep inspiration or during cough *(12–15)*.

Many methods of analgesia have been described to alleviate the postthoractomy pain and prevent the development of the postthoracotomy pain syndrome: modification of surgical technique, intercostal nerve block, intrapleural analgesia, lumbar and thoracic epidural, paravertebral block, intravenous narcotics together or without the use of nonsteroidal anti-inflammatory drugs (NSAIDS) *(5)*. A multimodal analgesic strategy that includes regional anesthesia is considered by some to be a gold standard for patients undergoing thoracotomy, and evidence suggests this may convey a morbidity benefit, although a clear improvement in outcomes after thoracotomy related to specific analgesic techniques has been difficult to prove *(7, 16)*.

SYSTEMIC TREATMENT OF PAIN

A multimodal approach to analgesia embraces the concept that intercepting signaling at numerous locations is more effective than targeting one site along the pain pathway *(7)*.

Opioids have been the mainstay of postoperative pain management for decades. Unfortunately, systemic opioids can be associated with significant side effects, which has prompted the search for alternative systemic medications *(4)*.

Nowdays, following systemic drugs can be used: opioids, NSAIDS, paracetamol, α2- adrenergic agonists (clonidine, dexmedetomidine), ketamine, local anaesthetics, gabapentin, pregabalin, magnesium, and anxiolytics *(4, 7)*.

EPIDURAL ANAESTHESIA AND ANALGESIA

The epidural administration of various anaesthetic and analgetic drugs gained increased popularity following the discovery of opioid receptors in the spinal cord capable of producing analgesia. The ability to produce neuroaxial anaesthesia and analgesia without dural puncture provides an attractive option. Epidural analgesia is defined as the intraoperative use of local anaesthetics, opioids and other drugs with analgetic properities.

Epidural analgesia has emerged as the analgesic technique of choice for postoperative thoracotomy pain management. Not only does the technique provide excellent pain control, but it also avoids much of the sedation associated with systemic opiates. Furthermore, the epidural catheter allows for continued dosing postoperatively, and avoids much of the motor blockade associated with intrathecal drug administration *(4)*. Continuous thoracic epidural catheter techniques have been widely studied and are currently considered the standard for analgesia in patients undergoing thoracic surgery *(4, 17)*.

Epidural analgesia is associated with a zone of differntial block. Epidural effect is not only analgesia, but also many other effects- cardiovascular, coagulation, pulmonary function, gastrointestinal system and stress response *(2)*. Epidural technique effectively blunt the stress response to surgery and provide superior pain relief compared to systemic opioids for patients undergoing thoracic surgery *(7)*.

Whereas there is evidence that suggests that epidural analgesia offers superior pain relief, not all studies have shown that epidural analgesia improves pulmonary function and reduces pulmonary complications *(18,19)*. Meta-analyses have also demonstrated reductions in bleeding, infections, respiratory depression, renal failure, and vascular complications *(7)*.

The risks of epidural placement should not be overlooked in evaluating the value of postoperative neuraxial analgesia, and such risks need to be discussed before undergoing any procedure. These include local anesthetic allergy, concentration-dependent neurotoxicity , inadvertent entry into the intrathecal space, nerve root injury and the risk of an epidural hematoma *(2, 7)*.

Major contraindication for epidural analgesia are: patient refusal, active infection at the site of needle insertion, presence of systhemic infection and sepsis and coagulation disorders. Other contraindication, like pre-existant neurologic deficit, respiratory failure, severe cardiac desease, increased intracranial pressure, lack of cooperation, are relative *(2)*.

Both lumbar and thoracic epidural catheters can be used for postoperative thoracotomy pain management. The superiority of thoracic epidural analgesia over lumbar epidural analgesia has been called into question. As a result of limited evidence confirming the benefits of thoracic versus lumbar epidural analgesia, some authors have expressed caution in using thoracic epidural analgesia on a routine basis *(4)*.

PARAVERTEBRAL BLOCK

Paravertebral blocks (PVB) produce unilateral trunk anaesthesia by blocking the segmental nerves of the spinal cord. PVB decrease cardiovascular and respiratory effects of epidural block. The paravertebral space is bounded by

the vertebral body medially, the transverse process and costotransverse ligament superficially and parietal pleura laterally. The lumbal paravertebral space is not countinous with thoracic. It contains the dorsal and ventral rami of the spinal roots as well as sympathetic fibres of the ventral rami. Thus anaesthetisc introduced into this space provide an unilateral motor, anaesthetics and sympathetic block *(2).*

Paravertebral blocks can be placed via a single injection or catheter-based continuous nerve blockade to achieve unilateral thoracic analgesia (2, 4, 7).

Over the past decade enthusiasm for a thoracic paravertebral blocks (TPB) in patients undergoing thoracic surgery has increased *(13).*

Several recent studies have suggested that paravertebral analgesia can be an effective alternative to epidural analgesia in thoracotomy patients *(4).* According to published studies paravertebral analgesia provide simular or better analgesia, the patient provide less postoperative morphine consumption and better preservation of pulmonary function. In addition, side effects such as nausea, vomiting, hypotension and urine retention were more problematic in the epidural group *(2, 4).* Paravertebral analgesia with levobupivacaine is very efficient in treatment of postoperative pain after thoracic surgery *(20).* The patients with paravertebral analgesia had better perioperative hemodynamic stability with less need for intravenous colloid therapy and vasopressor administration during open lung surgery *(21).*

The absolute and relative contraindications are the same as for epidural block *(2).* Compared to the other available regional techniques such as intercostals and interpleurals TPB offers better quality, longer duration of analgesia and less side effects *(13).*

INTERCOSTAL NERVE BLOCK

Blockade of intercostal nerves interrupts C-fiber afferent transmission of impulses to the spinal cord. A single intercostal injection of a long-acting local anesthetic can provide pain relief and improve pulmonary function for up to 6 hours *(4, 22).* Percutaneous intercostal blocks can be performed before surgery, or the surgeon can conduct intrathoracic intercostal blockade under direct vision before chest closure. To achieve longer durations of analgesia, a continuous extrapleural intercostal nerve block technique can be performed. Often, patients receiving intercostal blocks for analgesia after thoracotomy will require additional interventions to achieve adequate pain control. Intercostal analgesia should be instituted in patients who do not qualify for thoracic epidural analgesia *(4,7).*

INTRAPLEURAL ANALGESIA

Local anesthetic agents can also be administered through a catheter positioned inside the pleural cavity as another modality to anesthetize intercostal nerves. The mechanism of action appears to be diffusion across the parietal pleura *(23).*

Intrapleural analgesia is not as effective as epidural and paravertebral analgesia *(4).*

VIDEO-ASSISTED THORACIC SURGERY (VATS)

VATS is a type of thoracic surgery performed using a small video camera that is introduced into the patient's chest via a scope. It has been introduced in early 90s.

VATS has emerged as a minimal invasive technique for lung biopsy and resection of peripheral lung cancer. Benefits of the technique when compared with thoracotomy in lung cancer patients include improvement in postoperative pulmonary function, more rapid return to activity, shorter postoperative stay, shorter intraoperative time, and improved patient satisfaction *(4).*

The implications seem to be that VATS is associated with less postoperative pain and postoperative morbidity when compared with operations with a significantly greater level of surgical stimulation and tissue damage than in those with limited dissection *(4).*

Typically three incisions are used. Although perioperative pain may be lessened, chronic neuralgia is not uncommon for many patients, three incisions may not be necessary. Recent ly the single incision videoscopic lung resection method (UNIVATS) for performing lung resections was introduced *(24, 25).*

PHRENIC NERVE INFILTRATION

Patients undergoing thoracic surgery frequently complain of ipsilateral shoulder pain due to diaphragmatic irritation. This pain is often not covered with the band of analgesia achieved with epidural pain management.

Patients receiving phrenic nerve block with lidocaine had a significantly decreased incidence of ipsilateral shoulder pain and an overall reduction in pain score when compared with placebo infiltration *(26).*

INCISIONAL ADMINISTRATION OF LOCAL ANAESTHETICS

The catheter in surgical incision and aplications of local anaesthetics to it provide an efficient analgesia following port access heart surgery and does not increase the risk for wound infection and does not interfere with wound healing *(27).*

CONCLUSION

Multimodal pain management strategies can improve postoperative pain management while contributing other outcome benefits to our high-risk patient population.

Realistic expectations should be set with the patient preoperatively and patient education should include a discussion of the risks and benefits of epidural or paravertebral catheters, peripheral nerve blocks, and other analgesic medications.

Proper patient preparation and a comprehensive team approach to pain management, involving the surgeon and anesthesiologist, are vital for minimizing postoperative pain and morbidity and improving patient satisfaction.

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Regional anesthesia in children: indications and limitations

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Abstract

The goal of regional anesthesia in infants and children is perioperative and postoperative pain relief. The use of regional anesthesia and analgesia provide improvement in patient outcomes, and may be helpful in special situations, such as premature babies, patients with neuromuscular disorders or non-fasting children presenting for urgent surgery. Application of ilioinguinal and rectus sheath blocks, transverses abdominal plane blocks and wound infiltration with local anesthetics is commonly performed in combination with general anesthesia. Continuous central and perineural infusion of local anesthetics remains the technique of choice for prolonged major surgery or intense postoperative pain. Caudal block still remains the most important and safe technique. Introduction of nerve stimulators and lastly ultrasound guided regional anesthesia techniques reduced the risks and increase the benefits of this kind of anesthesia. The safety profile of regional anesthesia presented in surveys is superior with the very low incidence of serious complications. The aim is to find the safest technique for realizing the anesthesia and analgesia in children where a benefit overcomes the risk.

HISTORY OF PEDIATRIC REGIONAL ANESTHESIA

Regional anesthesia becomes very popular in pediatric population. Central nerve blocks, like spinal and caudal (epidural) blocks are widely used not only in modern European centers, but also in developing countries.

Regional techniques in children started more than 100 years ago, by August Bier in 1899, reported first spinal anesthesia applied in child *(1).* Few years later (1909) Gray published the first large scale series with spinal anesthesia in children undergoing various surgical interventions *(2).*

The second renaissance of regional anesthesia in children was in 1980s, in which period the concerns about risks of regional anesthesia were raised. However, performed scientific studies improve the beneficial effects of these techniques in infants and children *(3–5).*

The third period of regional anesthesia in children is his growing with technology developments. Introduction of nerve stimulators and lastly ultrasound guided regional anesthesia techniques reduced the risks and increase the benefits of this kind of anesthesia.

INDICATIONS FOR REGIONAL ANESTHESIA IN CHILDREN

Indications for regional anesthesia depend on the type of intervention, the age of child and the anesthetist's experience. This kind of an-

esthesia is widely used in urologic, orthopedic and lower abdominal surgery, and also in cardiac surgery. The other indications for this kind of anesthesia are the all cases in which is general anesthesia contraindicated, like full stomach and risk of aspiration, difficult intubation, allergy to general anesthesia, pseudocholynesterase deficiency or history of malignant hyperthermia. Regional anesthesia can be used in patients with upper airway or pulmonary infections.

The block selection is depended on age. In neonates and infants, two kinds of blocks are mostly used: spinal and caudal epidural. Peripheral nerve blocks are used in older children, mostly, below 6 years old.

When we talk about indications and benefits of regional anesthesia in pediatric population, we must compare it with general anesthesia.

Risk of morbidity and mortality is highest in children under 1 year of age during general anesthesia. However, most operations are avoided during this period; surgery performed on neonates is often emergency surgery. Anesthetic concerns relate mostly to the airway and cardiovascular systems, but some of the metabolic and neuromuscular disorders may have life-threatening reactions with anesthetic agents. The morbidity related to regional anesthesia in children, based on retrospective and prospective studies, is low, 1: 1000 overall *(6–9).*

Drugs used to generate general anesthesia have been used for many decades to patients of all ages without evidence of long-term damage. New evidence from animal research is accumulating in the field of anesthetic neurotoxicity *(10–12).* According to their results, possibility of long lasting effects on the central nervous system might be expected. Infants and neonates are considered to be at greater risk due to immature nervous systems. Reaching definite information about the effects of anesthetics on the developing brain will probably take numerous animal and human studies during many years. These further studies need to answer many questions regarding the effects of anesthetics on neurologic development in children other than age, the use of specific anesthetic drugs and techniques, duration of exposure, doses and other factors. Currently there are no alternatives to the anesthetic drugs in use, but application of regional anesthesia when possible may be the best alternative.

Surgical trauma induces a stress response that has endocrine, metabolic, hormonal, immunologic and inflammatory consequences. All these factors lead to cellular and organ dysfunctions with long convalescence period, especially in children. Regional anesthesia was more effective in reducing surgical stress during surgery than systemic opioids *(13).*

Respiratory complications during and after general anesthesia in babies are the other reason to practice regional anesthesia. Alveolar collapse, hypoxemia, apnea and bradycardia are significantly lower postoperative complications with regional blocks, than those who receive general anesthesia. Rate of ventilator support after anesthesia is also reduced, mostly in large surgeries, like thoracic, upper abdominal and cardiac anesthesia *(14, 15).*

Analgesia is in other issue achieved with regional blocks. Acute pain causes chest and abdominal wall muscle splinting and result with decreased tidal volume and alveolar ventilation *(16).* Pain in babies and small children has been ignored for many years, and usually was untreated. Quality of postoperative pain control possible with regional anesthesia and its minimal effect on cognitive function is difficult to realize with other methods. Neonates had lower pain scores and overdose with opioids could have fatal outcome *(17).*

Caudal blocks and dorsal penile blocks are effective for circumcision performed in awake neonates. Ilioinguinal and rectus sheath blocks, transverses abdominal plane blocks and wound infiltration with local anesthetics is commonly performed in combination with general anesthesia. Spinal, epidural, and caudal routes are applied for with general anesthesia or in awake neonates *(18).* The advantages include reduction of general anesthetic and opioid requirements, and the need for postoperative mechanical ventilation and other postoperative respiratory complications.

But still, when compared to adult regional anesthesia, regional anesthesia in children is relatively rarely done. According to a French survey, regional pediatric anesthesia represents 12% of the total anesthesia cases; infants represent 1%, and neonates or preterm babies are extremely rarely done *(19).*

In regards with many studies and meta-analyses *(20–21)* is improved that epidural analgesia decrease the length of stay in hospital, decrease the complications, like respiratory complications, vascular and gastrointestinal complications, low the rate of nausea and vomiting in postoperative period.

CONTINUAL REGIONAL ANESTHESIA

Prolonged intraoperative and postoperative analgesia with continuous central or peripheral nerve block catheters (CCT) became the preferred technique in many pediatric centers. Duration of plain long acting local anesthetics is only 3–5 h, which is easily solved by this technique.

The indications to place a catheter for continuous peripheral nerve blocks are long and painful intraoperative procedures requiring postoperative pain control for many days. Postoperative rehabilitation and physiotherapy are probably the main indications, because only if pain is under control, the successful rehabilitation could be performed. Many published studies underline the efficacy

and safety of analgesia via a peripheral catheter, and the low rate of complications or side effects. The stress response and postoperative complications is visibly decreased compared with systemic analgesia. They can affect outcome and the postoperative cost, intensive care unit and hospital stay is rapidly increased. The incidence of PONV is very low, but the bowel function is not impaired *(22).*

In neonates, epidural catheters inserted through the sacral hiatus can be advanced to a lumbar or thoracic level. This catheter allows the neonate to benefit from epidural analgesia without the worry of spinal cord injury *(23).* In the series of 15,013 central blocks; 29 of them was neuraxial catheters, the complication rate for 0±30-day-old term and preterm neonates was 0% *(19).*

The conduct of continual regional blocks in children by pediatric anesthesiologist carries only a small risk for neural damage *(19).*

LIMITATIONS OF REGIONAL ANESTHESIA IN CHILDREN

The anatomy of children differs from that of adults in the size and position of the spinal cord. At birth, the cord ends at L3 and the dura at S3; therefore, an injury to the spinal cord can occur when a lumbar epidural block is performed even at low levels. By the end of the first year of life, the cord and the dural sac rise to reach their adult levels, L1, L2 and S2. The loose epidural fat increases a spread of local anesthetics, up to the thoracic region. Up to the age of 6–8 years central nerve blocks, spinal and epidural, causes only minimal cardiovascular changes.

Myelination is not complete until 12 years of age. Incomplete myelination allows for better penetration of local anesthetic into the nerve fibers. Also, the loose of fascial attachments around the nerves increase the spread of local anesthetic. Furthermore, because the local anesthetic spreads easily in children, the duration of the block may be shortened compared to an adult. As the patient's age increases, local anesthetic latency of onset and duration of action increases as well *(24).*

Martin Jöhr *(25),* in his article presented at ESRA Winter Week 2010, described three phenomena which characterized the pharmacokinetics in neonates and small infants: firstly, a larger volume of distribution leading to lower plasma levels; secondly, an increased free non-protein bound fraction enhances toxicity and, thirdly, a diminished metabolic clearance. Low levels of α-1 acid glycoprotein lead to higher serum levels of unbound local anesthetic, and this free drug is responsible for toxicity. Infants also have decreased clearance and a longer elimination half-life of local anesthetic compared to adults. All these factors contribute to the increased general risk of local anesthetic toxicity resulting from a predominance of free drug circulating in the pediatric patient's plasma during regional anesthesia.

Absolute contraindications for spinal anesthesia in children include refusal of the parents, coagulation defects, and infection at the site of insertion, true allergy to local anesthetics, severe hypovolemia, progressive neurologic disease and uncontrolled convulsions *(26).*

The French-Language Society of Pediatric Anesthesiologists *(19)* reports the results during the one year period. From 85,412 procedures; 61,003 were realized with general anesthesia and only in 24,409 cases were performed regional anesthesia. Most of the blocks were caudal (15,013 or more than 60%), and the other part included different regional techniques. Most of the blocks were performed under light anesthesia. Complications were rare and minor, without any sequel. The overall complications rate of regional anesthesia was 0.9 in 1000, but complications occurred with central blocks were 1.5 in 1000.

The incidence of complications during regional anesthesia is relatively low.

CONCLUSIONS

Regional anesthesia could not replace the general anesthesia in children. But, the high benefits and extremely low incidence of complications during regional anesthesia must support anesthesiologists to use them more frequently.

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Regional anaesthesia in cancer surgery: an update

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Abbreviations:
ASA – American Society of Anesthesiologists
CMI – cell-mediated immunity
COX – cyclooxygenase
CWI – continuous wound infiltration
EA – epidural anaesthesia
IL – interleukin
NK – natural killer
PNB – peripheral nerve blocks
TAP – transversus abdominis plane
TNF – tumour necrosis factor

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Abstract

Anaesthetic techniques can influence the cellular immune system and affect long term outcome. Cancer surgery itself and general anaesthetics, especially opioids, suppress immunity and therefore promote metastases. Regional anaesthesia attenuates the immunosuppressive effect of surgery. Local anaesthetics, contrary to opioids, stimulate the activity of natural killer (NK) cells during the perioperative period. All techniques of regional anaesthesia are very useful and applicable in cancer surgery, either for the anaesthesia itself or for the treatment of postoperative pain. The relationship between regional anaesthesia and cancer recurrence is one of the most interesting topics in anaesthesia today, but we must wait the results of prospective trials before definitive conclusions.

INTRODUCTION

Cancer remains a significant cause of morbidity and mortality internationally. It is the second most common cause of death. The likelihood of tumour metastases depends on the balance between the metastatic potential of the tumour and the anti-metastatic host defences. Surgery is the mainstay treatment for solid tumours, but studies on humans have demonstrated that surgery itself can promote the development of metastases. The potential effect of anaesthesia on long-term patient outcome has been increasingly acknowledged *(1)*. The perioperative period is a critical time and the suppression of host defence mechanisms at that time can have deleterious long-term consequences. The perioperative stress response affects the immune system which has been developed to protect us from infection but also from cancer. Therefore, at the same time cancer surgery may initiate migration of cancer cells through the body and supress the defence immune system. The question that arises is how the choice of anaesthetic technique improves ability of body to eliminate cancer cells and upgrade survival.

PERIOPERATIVE IMMUNE RESPONSE AND CANCER

Animal studies indicate that immune response control over the circulation of tumour cells and micrometastasis is carried out mainly through cell-mediated immunity (CMI), which includes cytotoxic T lymphocytes, NK (natural killer) cells, NK-T cells, dendritic cells and macrophages *(2)*. NK cells are important because they can naturally recognise and kill malignant cells. B-adrenergic stimulation, which increases during stress states supresses NK activity and therefore promotes

metastasis *(3).* Human studies show that low perioperative levels of NK activity are associated with an increased cancer related morbidity and mortality *(4, 5).*

Cancer surgery supresses immunity and therefore promotes metastasis. Growth of pre-existing micro metastases and dissemination of malignant cells during postoperative period is facilitated *(6).* Further, surgical stress activates angiogenesis which contributes to neoplastic growth.

ROLE OF ANAESTESIA IN THE PEROPERATIVE IMMUNE RESPONSE AND CANCER

The choice of anaesthetic technique and drugs profoundly influences the immune response and consequently cancer metastasis. Melamed et al. demonstrated in rats that ketamine, thiopental and halothane reduces NK cell activity and increased lung tumour retention or lung metastasis *(7).* Propofol does not affect metastasis, which may be related to its B-adrenergic antagonist properties *(8).* Another study has been looked at propofol conjugates (propofol-docosahex-aenoate and propofol-eicosapentaenoate) as treatment for breast cancer, as they have been shown to inhibit cellular adhesion, migration and apoptosis in breast cancer cells. Effects of inhalation anaesthetics on tumour growth were studied by Brozovic et al. in mice. Their results confirmed the genotoxic and cytotoxic activity of halogenated inhalation anaesthetics on tumour cells *(9).* Isoflurane and halothane inhibit interferon stimulation of NK cell cytotoxicity in mice *(10).* Multiple studies have demonstrated *in vitro* effects that may have some relevance in the cancer setting. For instance, sevoflurane alters the release of cytokines (IL-1β and TNF-α, but not IL-2) by NK and NK-like cells *in vitro (11).* In humans, one large retrospective analysis found that general anaesthesia for excision of primary melanoma was associated with a decrease in the survival rate compared with local anaesthesia. The difference was attributed to use of general anaesthetic agents. General anaesthesia decreases circulating NK cells in patients undergoing elective orthopaedic surgery *(12).* Neutrophil, macrophage, dendritic and T-cell function are also impaired *(13).* Nitrous oxide interferes with DNA, purine and thymidylate synthesis and depressed neutrophil chemotaxis *(14).* Opioid administration has been shown to suppress cell-mediated and humoral immunity. This includes NK cell activity, production of immune-stimulating cytokines, phagocytic activity and antibody production *(13, 15).* Morphine at clinically relevant doses increases angiogenesis and promotes breast tumour growth in mice *(16).* Tramadol, which has noradrenergic and serotonergic activity, stimulates NK cell activity, both in rodents and humans *(17).* The differences between morphine and tramadol have been shown in humans undergoing hysterectomy for uterine carcinoma. T-lymphocyte proliferation was depressed in both groups, but remained depressed only in morphine group. Neither surgery nor morphine affected NK cell activity, whereas tramadol was shown to enhance NK cell activity. Long term outcome was not reported *(18).*

Non-steroidal anti-inflammatory drugs inhibit prostaglandin synthesis via inhibition of the cyclooxygenase (COX) enzyme. Tumour cells have been shown to secrete prostaglandins, and this may be a mechanism to evade host cell-mediated immunity *(19).*

When we analyse the effects of regional anaesthesia, we can find two major retrospective studies. One showed a 57% reduction in incidence of biochemical cancer recurrence when epidural analgesia was used for open prostatectomy when compared with postoperative opioid analgesia. The other showed a four-fold reduction in the incidence of recurrence or metastasis in patients who received general and paravertebral anaesthesia and analgesia when compared with general anaesthesia and morphine analgesia for breast cancer surgery *(20).* The effect of regional anaesthesia on human breast cancer cells in vitro has also been investigated. Serum from patients who received propofol/ paravertebral anaesthesia was found to inhibit proliferation but not migration of an oestrogen receptor-negative breast cancer cell line when compared with a sevoflurane/ opioid group *(21).*

The potential ability of regional anaesthesia to improve long-term outcome after cancer surgery can be attributed to at least three different mechanisms. First, regional anaesthesia attenuates the immunosuppressive effect of surgery. Secondly, patients who received regional analgesia have lower opioid requirements. Opioids may themselves inhibit cell-mediated immunity and host anti-tumour defences. Finally, when regional anaesthesia is used in addition to general anaesthesia, the amount of general anaesthetic required during surgery is reduced. Further, local anaesthetics contrary to opioids stimulate the activity of NK cells during the perioperative period. Intravenous infusion of lidocaine reduces surgery-induced immune alterations. The long-term clinical implications of these findings are unknown and warrant future investigations *(13).* Acute pain suppressed NK cell activity too. Optimizing postoperative pain management may attenuate the post-surgical inhibition of host anti-tumour defence mechanism, including NK cells.

Postoperative pain therapy may play a very important role in metastasis after cancer surgery. Page et al. demonstrated in rats that the provision of pain relief attenuates the surgery-induced increase in metastatic susceptibility, likely because of reduction in the stress response. They demonstrated that preoperative intrathecal administration of bupivacaine plus morphine and the perioperative systemic administration of fentanyl significantly enhanced the host resistance to surgery-induced increases in lung metastasis. They suggested that the pain-alleviating

effect of these drugs attenuated the surgery-induced promotion of metastasis rather than having direct effect on immunity, tumour cells or other mechanisms *(22).*

Opioids likely play a profoundly negative role. Morphine has been repeatedly shown to promote angiogenesis. It is well established that opioids inhibit cellular and humoral immune function in humans.

Anaesthetic strategies that protect the immune system have been suggested to guard against this effect and may reduce cancer recurrence and improve length of survival. Regional anaesthesia has been shown to minimise immunosuppression via its opioid sparing effect and by reducing the response to surgical stress.

There are many conflicting studies regarding regional anaesthesia and its impact on cancer recurrence. It has been reported that regional anaesthesia decreases some of the risk factors that promote cancer metastasis by attenuating the neuroendocrine stress response to surgery, reducing pain, the need for general anaesthetics, minimizing opioid use and decreasing pro-inflammatory cytokines. The theory is that regional anaesthesia may leave an intact immune system which could potentially decrease cancer recurrence via endogenous removal of tumour cell microemboli. A large analysis of 42 000 patients with colon cancer who underwent colon resection demonstrated that epidural use was associated with 5-year improved overall survival, but not actual cancer recurrence *(23).*

However, more prospective randomised controlled clinical trials are necessary to statistically demonstrate a causal relationship between regional anaesthesia and cancer recurrence. In general, all techniques of regional anaesthesia are very useful and applicable in cancer surgery, either for the anaesthesia itself or for the treatment of postoperative pain. We previously mentioned the benefits of thoracic paravertebral block for breast surgery and its influence on the cancer recurrence. However, this technique has the potential to offer long-lasting pain relief and reduce postoperative nausea, vomiting and chronic pain. Paravertebral block can uniquely eliminate cortical responses to thoracic dermatomes stimulation *(24).*

The results of studies aimed on application of epidural anaesthesia (EA) in large abdominal surgery are controversial. Although EA is theoretically supposed to be a favourable immune-modulating intervention, not all studies show a consistent beneficial effect from EA in colon cancer patients. There is increasing evidence deriving from animal studies thoracic epidural blockade could have an important role in modifying tissue microperfusion and protecting microcirculatory weak units from ischemic damage, regardless of the effect on macro-haemodynamics. Continuous EA is a technique that ensures quality analgesia for surgery in the upper abdomen. Its advantages are reduction of opioid consumption, lower incidence of cardiac and pulmonary complications, shorter duration of postoperative ileus and early mobilisation of patients *(25).* Christopherson et al. found a better overall survival in the first 1.5 post-operative years in 177 colon cancer patients for stage I-II patients with a mean age of 69 years old who received EA. Nevertheless, the type of anaesthesia did not appear to affect long-term survival *(26).* A significant better overall survival was found by Holler et al. The positive impact of this study was the most significant in the high-risk patients (American Society of Anesthesiologists (ASA) score 3-4) *(27).* The Swedish study of Gupta et al. found a reduction in all-cause mortality in rectal cancer patients who received EA *(28).* Contrary, the study of Myles et al. suggested that the use of epidural block in abdominal surgery for cancer is not associated with improved cancer-free survival *(29).* Study of Hiller et al. considered that effective epidural analgesia improves cancer outcomes following gastro-oesophageal cancer surgery in patients with grouped pathological staging *(30).* Continuous EA is a technique that ensures quality analgesia for surgery in the upper abdomen. The advantages of EA are reduced opioid consumption, lower incidence of cardiac and pulmonary complications, and shorter duration of postoperative ileus and early mobilisation of patients. However, there are some limitations in the use of EA in the liver surgery such as postoperative coagulation disorders.

Contrary to EA continuous wound infiltration (CWI) is analgesic technique of application local anaesthetic directly into surgical wound through multi-holed wound catheter placed by surgeon on the end of the surgery. CWI enables reduction in opioid consumption and opioid related side effects, earlier recovery of bowel function and hospital stay. Continuous wound infusion of local anaesthetics has been successfully applied for postoperative pain control in several procedures but, it is underused in thoracic surgery. Fiorelli et al. in their paper concluded that CWI is an effective, easy and safe procedure. It significantly reduces systemic inflammatory markers, pain scores and opioid intake; and accelerates the recovery of respiratory function *(31).*

In ovarian cancer patients intraoperative use of epidural anaesthesia was associated with an increased time to tumour recurrence after surgery *(32).* Quality improvement in colorectal and gynaecological surgery is performing the transversus abdominis plane (TAP) block. Adding TAP block is appropriate tool to improve patient and financial outcomes and to achieve better results of treatment. Keller and colleges analysed results of 200 patients with colorectal carcinoma and concluded that transverses abdominis plane blocks may be an efficient, cost-effective method for improving laparoscopic colorectal surgery *(33).*

Peripheral nerve blocks (PNB) or plexus blocks can be used when pain occurs in the area of one or more periph-

eral nerves. The pain may arise from primary or secondary tumor deposits or be the result of treatment or secondary complications such as pathological fracture or vascular occlusion. PNB are often used to avoid side effects and complications of general anaesthesia, particularly respiratory-related effects, and to provide analgesia while minimizing opioid use. PNB are widely-used for surgical anaesthesia as well as for postoperative pain control, and offer distinct benefits over general or central blocks in certain clinical situations. Further, PNB provide analgesia that may be superior to other techniques for some patients. Koshy et al. described successful continuous femoral block for pain relief of acute severe cancer related pain caused by pathological femur fracture *(34)*. Locoregional anaesthesia provides better pain control, eliminating the need for opioids in the postoperative period and resulting in negative effects on immune function and tumour growth; it also reduces the release of endogenous opioids *(35)*.

CONCLUSION

Finally, we could conclude that the relationship between regional anaesthesia and cancer recurrence is one of the most interesting topics in anaesthesia today. The concept that anaesthesia can influence the outcome of cancer would raise our speciality to a new level. We must wait the results of prospective trials before definitive conclusions.

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Pain management in critically ill patients

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Abstract

Pain is a common and distressing symptom in intensive care unit (ICU) patients and despite of pain research, guideline development, numerous awareness campaigns and intense educational efforts, it remains currently under evaluated and undertreated. The pain relief in critically ill patients may be difficult to achieve due to complex interplay between mechanisms of critical illness, drug interactions, organ dysfunctions and factors involved in influencing pain perception. A different medications have been proposed for pain control and they have unique considerations when contemplated for use in the critically ill patient.

The purpose of this article is to provide an overview of most important pharmacologic pain treatment in the critically ill patient.

INTRODUCTION

Pain is a common and distressing symptom in intensive care unit (ICU) patients and represents a major clinical, social, and economic problem. It has been reported that almost 80% of patients experience different intensities of pain during their intensive care unit stay and identify it as one of the greatest sources of stress *(1, 2)*.

Such pain is problematic because produces adverse psychological and physiological response that includes increased heart rate, blood pressure, respiratory rate, neuroendocrine secretion and psychological distress. Failure to relieve pain produces a prolonged stress state, which can result in harmful multisystem effects and can therefore impair a patients recovery and discharge *(3)*. The primary goal of acute pain management in ICU patients are pain control and attenuation of the negative physiologic and psychological consequences of unrelieved pain. Although, a number of recent surveys, reported that enhanced pain management was associated with improved patient outcome in the ICU *(4, 5)* and despite of pain research, guideline development, numerous awareness campaigns and intense educational efforts, pain remains currently under evaluated and undertreated in patients who are critically ill *(6)*. Therefore, the importance of quality pain management in the ICU is inherently compelling and highly challenging.

Etiology and pain assessment in ICU patients

Although, adequate pain control is a basic human right *(6)*, a number of factors complicate the management of pain in the critically ill patient. In particular, critically ill patients may experience pain due to their underlying disease or surgery, but also it may be result of various and painful medical procedures (procedural pain) such as inserting urinary catheter, nasogastric tube, chest tubes, tracheal suctioning, invasive

lines, (arterial and central venous catheter) suture removal and routine nursing care. Nursing care procedures such as bathing, massage of back and pressure points, sheets change and repositioning are the most common painful procedures in ICU patients *(7)* Vazquez M *et al. (8)* analyzing pain intensity during 330 turnings in 96 medical-surgical patients and reported significantly increased pain score between rest and turning. The bolus of analgesic was used in less than 15% of the turnings. Further, although some ICU patients may be able to communicate, many critically ill patient with cognitive or communication problems due to stroke or brain injury, dementia, confusion, mechanical ventilation and concomitant use of sedatives, may have difficulty in reporting pain. Presence of the some causes mentioned above increases the likelihood for poor pain management, and worsens a patient's experience of pain. The first step in providing adequate pain relief for ICU patients is appropriate assessment. Pain should be assessed by self-reporting scales in patients able to communicate, or by behavioral pain scores in patients unable to communicate. Even though various self-report pain scales and behavioral pain scales specifically developed for use in critically ill adults are available, these are not always routinely used in the ICU. Patients'self-reporting of their pain is the gold standard of pain assessment and provides the most valid measurement of pain *(9).* The most widely used pain intensity scales are the Numeric Rating Scale (NRS) and Visual Analogue Scale (VAS) while Behavioral Pain Scale (BPS) is considered to be an alternative tool for assessing pain in critically ill, sedated, and mechanically ventilated patients. The BPS assesses pain through evaluation of facial expression, upper limb movements, and compliance with mechanical ventilation. A similar behavioral scale called the Critical-Care Pain Observation Tool (CPOT) may also be used.

Route of administration

The route of medication administration is an important consideration for the pharmacologic management of pain in the ICU setting. Intravenous administration is more commonly the route of choice in critically ill patients because of altered GI tract function that could lead to unpredictable absorption of medication.

The choice of intermittent vs. continuous infusion IV administration depends on factors such as the frequency and severity of pain, and the pharmacokinetics of the pain medication. The administration in bolus is associated with the variation in the peak plasma concentration, since the infusion maintains a more stable concentration, but can lead to accumulation of medication especially in patients with renal or liver failure.

Patient-controlled analgesia (PCA) is an effective method for administering analgesic medication and gives patients a sense of control over their pain, expecialiy in postoperative settings. Patients can determine when and how much medication they receive, regardless of analgesic technique. However, this technique requires fully conscious and orientated patients which make use of PCA limited in ICU patients.

Intravenous administration is generally preferred over subcutaneous or intramuscular routes given potentially inadequate absorption due to regional hypoperfusion (e.g., shock, subcutaneous edema). Regional or neuraxial (spinal or epidural) modalities may also be used in ICU following selected patients and selected surgical procedures. Epidural analgesia (EA) is probably the most often used regional anaesthetic technique in the ICU. EA should be proposed in critically ill patients, such as post-operative after thoracic, abdominal surgery, major vascular surgery and orthopedic surgery or trauma patients, typically.

The major disadvantages of epidural analgesia are the rare but catastrophic complications such as infection, epidural hematoma formation and nerve damage, which can occurred in ICU patients who have a high risk of developing these complications *(10).*

Pharmacotherapy

In January 2013, The Society of Critical Care Medicine (SCCM) published the Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit *(11).* Table 1. shows the commonly used pain management drugs and recommended doses. There are no data to support the preference of analgesic over the other.

Opioids

Opioids are the primary medications for managing pain in critically ill patients because of potency, concomitant mild sedative and anxiolytic properties, and their ability to be administered by multiple routes. Recommended opioids include fentanyl, remifentanil, morphine, and hydromorphone. The choice of opioid and the dosing regimen should be individualized based on drug's potency, pharmacokinetics and pharmacodynamic profiles, side effect profile, patient comorbidities, and function of specific organ systems, in particular the liver and kidneys.

Morphine sulfate is the most frequently used opioid in the ICU and has been traditionally a first-line opioid for the treatment of severe pain. Morphine has a half-life of 1.5 to 2h after intravenous administration in normal subjects, but in ICU patient, distribution volume and protein binding may be abnormal. Therefore, the patients can respond very differently to morphine doses in terms of the analgesic effect but also in terms of the side effects. Although, morphine, such as all opioids, may lead to respiratory depression, it is noteworthy to point out that the morphine-6-glucuronide metabolite is more potent than morphine itself, and that accumulation can occur, espe-

cially in patients with renal impairment. Therefore, morphine use should be avoided for patients with known renal insufficiency or failure. Side effects include histamine release, sedation, nausea, ileus, constipation, and spasm of the sphincter of Oddi. Morphine sulfate should be administered intravenously and titrated to effect. The loading dose of 0.05 mg/kg (2–5 mg) should be given over 5 to 15 min. In most patients, the average maintenance dose is 4 to 6 mg/h and should be administered at the dosing interval of 1–2 hrs. Continuous IV morphine can be administered with an initial 2–5 mg bolus dose followed by 1 mg/h.

Fentanyl is synthetic opioid roughly 100 times the potency of morphine, which does not cause histamine release and was preferred analgesic agent for critically ill patients with hemodynamic instability. It efficacy is due to its lipid solubility (600 times more lipid soluble than morphine), so if used > 4 hrs fentanyl must be used in the lowest tolerated dose to prevent prolonged effects. With prolonged infusion, the half-life increases dramatically from 30 – 60 minutes to 9–16 h and care must be taken to adjust infusion rate with time.

Fentanyl causes only minor hemodynamic changes and does not affect cardiac inotropy. The dose range for fentanyl infusions is variable and some patients may require higher doses. Bolus dose of 25–100 μg, with subsequent doses of 0.25–0.5 μg/kg every 15–30 minutes might be a good first alternative to morphine in treating acute painful conditions. Alternatively, a bolus dose of 1–2 mcg/kg (25–100 mcg) may be administered followed by initiation of the continuous infusion. Most patients will be adequately treated with 1 to 2 μg/kg/hr (25–200 μg/h infusion).

Remifentanil is a fast-acting drug and presents an equally fast recovery *(11)*. It is 150 –200 times more potent than morphine. Its metabolism does not depend on the liver. Analgesia-based sedation with remifentanil is a useful option for mechanically ventilated patients and it can be used in patients that need frequent neurological assessment. Studies have shown a shorter duration of mechanical ventilation and quicker ICU discharge with remifentanil compared with other opioids *(12, 13)*. It offers precise control of analgesia for painful procedures in ICU patients and has a highly predictable onset and offset, with a stable context sensitive half-time (3–10 min). No need for initial dose adjustment is required for patients with impaired renal and hepatic function. Therefore, analgesia-based sedation with remifentanil has been introduced as an option in ICU patients. Remifentanil can be administrated in higher doses than are normally used with other opioids without concerns about accumulation and the possibility of unpredictable and/or delayed recovery. Most ICU patients can be managed without bolus doses; if required, a bolus of 0.5–1 μg/kg is usually sufficient. It is recommended that remifentanil infusions should be started at 6–9 μg/kg/h and than titrated in the range dose 0.5–15 μg/kg/h. Some authors recommended dose to 60 μg/kg/h *(14)*. Even under these controlled conditions, this practice has not found widespread use because of the associated incidence of hypotension and bradycardia.

Hydromorphone is a semisynthetic opioid agonist that, like fentanyl, has a more rapid onset of analgesia (within 30 minutes) and a short half-life (2–4 hours). While the duration of action is similar to morphine, it does not stimulate histamine release. Hydromorphone is primarily metabolized in the liver to an active metabolite – hidromorphone-3-glucuronide, but it is not clinically significant. Hydromorphone is potent respiratory depressant and may accumulate in patients with renal failure, resulting in neuroexcitation and cognitive impairment. Dosing begins at 0.2 to 0.6 mg and titrated by 0.5 mg increments. Most patients requiring 1 to 2 mg every 1 to 2 hrs. In addition, if given as an intravenous continuous infusion the dose should be 0,5 –3 mg/h.

Tramadol is a centrally acting opioid-like drug, and acts by binding to the μ opiate receptor where it is a pure agonist like morphine and inhibits adrenaline and serotonin re–uptake. It is used to treat moderate to severe pain. The most common adverse effect is typical to other opioids and includes nausea, vomiting, dizziness drowsiness, dry mouth and headache. However, tramadol produces less respiratory and cardiovascular depression than morphine, and euphoria and constipation are also less common.

Recommended dosage of 100 mg can be administered as an initial bolus. During the 90 minutes following the initial bolus further doses of 50 mg may be given every 30 minutes, up to a total dose of 250 mg including the initial bolus. Subsequent doses should be 50 mg or 100 mg 4 to 6 hourly up to a total daily dose of 400 mg.

Non-opioid analgesics

Non-opioid analgesics are indicated for use in management of mild to moderate pain and moderate to severe pain with adjunctive opioid analgesics. Potential advantages of multimodal analgesia, that involves combination of analgesics with different mechanisms of action, include improved analgesia, effective analgesia with lower opioid doses, and decreased risk of opioid-related adverse effects.

Nonsteroidal anti-inflammatory drugs (NSAIDs) have opioid sparing effect but this has not been sufficiently investigated in ICU patients. Although the use of NSAIDs is still contraversial, they may be used as adjuncts to opioid therapy. The most common side effect include gastrointestinal bleeding, renal dysfunction and inhibition of platelet function.

All parenteral NSAIDs should be avoided in patients with preexisting renal insufficiency, asthma, hypoperfu-

TABLE 1
Commonly used pain management drugs and recommended doses.

Drug	Elimination Half-Life	Peak Effect (IV)	Suggested Dosage	Comments
Morphine	2-4 h	30 min	2-5 mg bolus 1-10 mg/h infusion	Avoid in hemodynamically unstable patients. Active metabolite accumulates in renal dysfunction. May cause itching due to histamine release.
Fentanyl	2-5 h	4 min	25-100 µg bolus 25-200 µg/h infusion	Fastest onset and shortest duration. Accumulation with hepatic impairment. Muscle rigidity.
Remifentanil	3-10 min	1-3 min	0.5-1 mcg/kg IV bolus 0.5-15 µg/kg/h infusion	No accumulation in hepatic/renal failure. Use IBW if body weight >130% IBW
Hydro-morphone	2-4 h	20 min	0.5-2 mg bolus and 0.2 to 0.6 mg every 1-2 h intermittent 0.5-3 mg/h infusion	Therapeutic option in patients tolerant to morphine/ fentanyl. Accumulation with hepatic/renal impairment 5-10x more potent than morphine.
Tramadol	5-6 h	45 min	100 mg bolus and 50 mg every 30 min up to 250 mg including the initial bolus. total daily dose of 400 mg.	The elimination of tramadol may be prolonged in hepatic/renal impairment Contraindicated in patients on MAOI or epilepsy.
Acetamino-phen	2-3 h	15 min	1 g every 6 h	May cause hypotension when given by infusion and may cause liver and kidney damage, when taken at higher than recommended doses (overdose).
Lidocaine	1,5-2 h	45-90 s	100 mg or 1.5–2 mg/kg at least half an hour before surgical incision, followed by an infusion of 1.33–3 mg/kg/h intraoperatively	Avoid in patients with arrhythmias, heart failure, coronary artery disease, Adams-Stokes, or heart blocks. Caution should be taken in patients with hepatic or renal failure, sinus bradycardia and incomplete branch block.

sion, advanced age, concomitant use of steroids and anticoagulants, situations that are frequently observed in ICU patients *(15)*. Treatment should be limited to the minimum dosage for the shortest possible time, not to exceed five days.

Acetaminophen (paracetamol) was approved for intravenous use in 2010 and is commonly administered for the short-term treatment of mild to moderate pain and febrile critically ill patients with infection. It differs from the available opioids and NSAIDs, since paracetamol does not increase incidence of nausea, vomiting, and respiratory depression that can occur with opioids, or the platelet dysfunction, gastritis, and renal toxicity that are associated with NSAIDs. Although, represents a relatively good safety profile, there is limited information regarding IV use in critically ill patients. Research to date has described that paracetamol can cause transient abnormalities of liver function and may cause hypotension in critically ill patients *(16)*. Acute liver failure is the most serious potential complication of the use of paracetamol. The key criteria for assessing potential hepatotoxicity with conventional doses of paracetamol may include hypoxic injury, altered pharmacokinetics, relative over-dosage, muscle glutathione depletion, malnutrition, dehydration, older age and alcoholism which is often seen in critically ill patients. The British National Formulary (BNF) suggests to administer a maximum daily infusion dose of 3 g in adults in these patient groups *(17)*.

Randomised, placebo-controlled trial that investigating the safety and efficacy of paracetamol in febrile ICU patients with known or suspected infection is currently underway study (the HEAT -Permissive HyperthErmiA Through Avoidance of Paracetamol in Known or Suspected Infection in the Intensive Care Unit) *(18)*. The results of this trial are expected to publish in early 2015 and should provide essential information on efficacy and safety of paracetamol in febrile critically ill patients. The recommended dose for IV acetaminophen is 1 g every 6 h with a maximum allowable dose of 4 g/daily.

Lidocaine is commonly used for regional anesthesia and nerve blocks, however, recent clinical studies demonstrated that intravenous perioperative administration of lidocaine can lead to better postoperative analgesia, reduced opioid consumption, improved intestinal motility and decrease hospital length of stay *(19, 20)*. Although, the analgesic effect depend on dose, there is considerable individual variability in pharmacokinetic response to lidocaine infusions. Serum steady state is achieved following a bolus of 1.5–2.0 mg/kg of lidocaine and infusion rates of 0.9–3.6 mg/kg/h. These doses generally result in plasma levels of 1.3–3.7 µg/ml, which provide a small

marigin of safety. Large doses have better analgesic effect but induce systemic lidocaine's toxicity. Lidocaine induces analgesia when serum ranges are kept at 1–5 μg/m. Although the half-life of the drug is only 120 minutes, the analgesia provided by systemic lidocaine is prolonged, over days or even weeks. With regard to analgesia, it has been reported that intravenous lidocaine produces three different pain relief stages: the first is during infusion and 30 to 60 minutes after its end; the second is a transient stage approximately 6h after infusion; and the third stage appears 24 to 48h after infusion and continues for 21 to 47 days *(21).* Intravenous lidocaine should not be used in patients with arrhythmias, heart failure, coronary artery disease, Adams-Stokes, or heart blocks. Caution should be taken also when using lidocaine in patients with hepatic or renal failure, sinus bradycardia, and incomplete branch block since possible accumulation of lidocaine or its metabolites may lead to toxic phenomena.

Although there is no clear consensus on the dosage regimen, many studies have used a bolus dose of 100 mg or 1.5 mg/kg at least half an hour before surgical incision, followed by an infusion of 1.33–3 mg/kg/h intraoperatively and continued after operation variably up to 24 h. The application of continuous lidocaine has not been documented in the ICU in controlled studies and more study is needed to confirm beneficial effects of lidocaine in critically ill patients.

Regional anesthesia and analgesia

Regional anesthesia and analgesia although, not commonly used as a primary modality for analgesia in critically ill patients, can help to improve respiratory and bowel function, mental status and patient comfort secondary to its opioid-sparing effects. It minimizes patient discomfort and reduces the physiological and psychological stress, as in non-critical patients. Limitations for the use of regional anesthetic techniques are mainly associated with bleeding risks, coagulation disorders, hemodynamic disturbances and difficulties in neurologic assessment. The use of regional analgesia in the ICU settings should evaluate the risk and benefits due to limited cooperation of the patient, and the indication for it use should be carefully assessed regarding to patients clinical condition.

As mentioned above, epidural analgesia is probably the regional anaesthetic technique most often used in the ICU, but nerve blocks and other sophisticated techniques started in the operating room may also be used for pain relief in critically ill patients and should not be discontinued when the patient is transferred to ICU.

CONCLUSION

Pain management is an essential component of quality care delivery for the critically ill patient. The patients in ICU often suffer from undertreated and unrecognized pain, with potentially serious physical and psychological effects. The availability of a wide range of treatment options together with the recognized importance of adequate management enables better understand, evaluate and manage pain in the critically ill patient. It's therefore important for clinicians to recognize a patient's pain profile and rational choice of pain medication should be based upon individual needs and desired effect of analgesic. Effective pain management is a moral imperative and professional responsibility for both doctors and nurses.

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Neuropathic orofacial pain – diagnostic and therapeutic challenges

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Abbreviations:

CNS	– Central nervous system
DN4	– Neuropathic Pain Diagnostic Questionnaire
EFIC	– The European Pain Federation
IHS	– The International Headache Society
IASP	– The International Association for the Study of Pain
ICHD-3	– 3rd International Classification of Headache Disorders
LANSS	– The Leeds Assessment of Neuropathic Symptoms and Signs
NPQ	– Neuropathic Pain Questionnaire
NSAIDs	– non-steroidal anti-inflammatory drugs
OFP	– Chronic neuropathic orofacial pain
PHN	– postherpetic neuralgia
SSNRIs	– selective serotonin norepinephrine reuptake inhibitors
SSRIs	– selective serotonin reuptake inhibitors
TAD	– tricyclic antidepressants
TN	– trigeminal neuralgia

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Abstract

Chronic neuropathic orofacial pain (OFP) is the leading symptom for a wide range of conditions. It can exist independently of any addition signs, symptoms and radiological or laboratory abnormalities. In addition to physical suffering, OFP causes emotional, psychological and social disturbances and thus significantly influences the quality of life of those affected. Several key factors make OFP a complex diagnostic and therapeutic challenge. These include a lack of diagnostic criteria that are both validated and readily applicable in clinical settings and a lack of sufficient education about pain in undergraduate medical training programs. There is also a need to develop more analgesic therapies offering improved efficacy and side effect profiles. Finally, the provision of analgesic therapies by health insurance programs need to be harmonized with the most current evidence-based treatment protocols. In addition to offering recommendations in these areas, this paper provides an overview of the most common clinical forms of nonodontogenic OFP, epidemiological data, and current diagnostic and therapeutic options.

INTRODUCTION

Pain is one of the most unpleasant aspects of many diseases. To underscore the importance of pain as a global health problem, the International Association for the Study of Pain (IASP) launched its first "Global Year Against Pain," in 2004 with the slogan; *Pain management should be a human right*. Each IASP annual campaign is dedicated to the study of pain arising from particular conditions or etiologies. For example, 2013 marked the year against chronic pain, whereas orofacial pain was the focus in 2014, which was followed by a year against neuropathic pain in 2015 *(1)*. Such campaigns help raise awareness for the many ways in which various types of pain effect health, ranging from a vital warning sign to a debilitating condition. Acute pain, which signals the occurrence of injury or disease, provides an important protective function. Conversely, chronic pain provides no real or potential benefits, resulting only in unnecessary suffering. This is particularly true of neuropathic pain, an important component of numerous medical conditions *(2)*. Whatever its origin, pain is recognized globally as one of the primary reasons for seeking medical attention. The pain suffered by individuals creates not only personal but also societal costs. Communities are burdened with both the direct costs of healthcare utilization and the indirect costs of reduced worker productivity and increased absenteeism due to pain.

One of the most significant sources of pain in the human body is the orofacial region, a highly sensitive area with abundant pain receptors (3).

The orofacial region also has great psychological significance as the center for chewing, swallowing, speech production, communication and personal expression *(4)*. Therefore, chronic pain is associated with additional emotional, psychological and social disturbances when located in the orofacial region. These changes significantly affect the quality of life of those living with chronic orofacial pain (OFP) *(5)*. The global prevalence of orofacial pain is estimated at 17–26%, with 7–11% of patients experiencing chronic OFP *(6)*. It is not known what share of this percentage is attributable to neuropathic pain, an important causative factor in many OFP conditions. The prevalence of orofacial and chronic pain can reasonably be expected to increase as demographics shift toward longer life expectancies. An aging population includes an increased number of patients living with chronic and painful conditions such as diabetes and cancer. Aging also results in increased exposure to therapeutic methods for these and other conditions that can result in neuropathic pain. Such an increasing potential for chronic and orofacial pain creates the need to consider a range of likely consequences, not least of which is the impact on quality of life *(6, 7)*.

The causes and mechanisms of chronic pain are not entirely clear, although risk and precipitating factors have been identified for the majority of conditions. A large body of evidence shows that pain is often inadequately treated. Over time, continuous pain symptoms alter neuroplasticity and may cause hyperexcitability, changes that lead to the development of chronic pain *(5)*. Thus, unabated neuropathic pain can become a neurological disorder or dysfunction of the central nervous system (CNS), in much the same way as epilepsy or Parkinson's disease. These changes to the CNS pain signaling pathways hinder the effectiveness of therapies aimed at alleviating the symptoms of chronic pain.

Nonodontogenic neuropathic orofacial pain

A diagnosis of nonodontogenic neuropathic orofacial pain can only be made after eliminating the teeth as the potential source of pain. Odontogenic OFP arises from tooth damage or decay and is often localized to the oral cavity. It can also occur in the region of the face that is above the neck, in front of the ears, and below the orbitomeatal line. If dental caries, poor fillings, trauma, and dental fractures have all been eliminated as the source of pain, OFP is considered unrelated to teeth and is therefore referred to as nonodontogenic. Additional findings related to the distribution and timing of pain may help confirm its origin. Nonodontogenic pain is often treatment resistant, even with the use of local anesthetics and is prone to developing into a chronic condition *(8)*. Additionally, pain that is bilateral or simultaneously encompasses multiple teeth is likely to be of a nonodontogenic origin *(9)*.

Nonodontogenic neuropathic OFP shares many of the characteristic features recognized in other forms of neuropathy. Neuropathic pain arises from peripheral and central changes in neuronal function that are perceived as persistent pain and sensory abnormalities. Permanent loss or injury of primary afferent fibers, a process referred to as deafferentation, results in peripheral neuropathic pain. Central neuropathic pain, however, arises from direct damage to the structure of the central nervous system *(10)*. The timing and duration of symptoms are characteristic of neuropathic pain, which can be both episodic (or *paroxysmal*) and continuous. While some patients experience complete relief from pain symptoms between episodes, others can experience paroxysms of pain as an acute exacerbation of an otherwise continuous pain syndrome (4). While some causes of OFP may be difficult to discern, a careful history including the duration and nature of symptoms can pinpoint a likely etiology. For example, pain described as continuous and burning is typical of neuritis and post-traumatic neuropathy. Neuropathy most often manifests as repeated, episodic attacks of short stabbing or shooting pain. The onset of these episodes can be either spontaneous (or *stimulus independent*) or provoked by stimuli. Pain is intensified by the stimulation of trigger-points or individual muscles. Pain can also be increased by emotional stress, physical activity, changes in the position of the head and so on. Neuropathic pain is often accompanied by additional sensory signs and symptoms such as allodynia, pain provoked by a stimulus (as a light touch of the skin) which would not normally provoke pain. Thermal and mechanical stimuli are the types most often associated with provoking allodynia. Hyperalgesia, an increased sensitivity to painful stimuli, is another characteristic positive sign. Negative signs, such as hypoalgesia and hypoesthesia, can also indicate a neuropathic etiology. While many of these signs can be elucidated from patient history, the full range of sensory changes experience by an individual patient is best assessed using quantitative sensory testing. This non-invasive method relies on the selective response of specific types of nerve fibers to particular stimuli. Given that A-beta fibers are selectively stimulated by electricity, A-delta fibers respond to cold or punctate mechanical stimuli and C-fibers are stimulated by heat, these types of stimuli are applied externally to selectively stimulate and record a response from each type of nerve fiber. The area from which neuropathic pain and sensory changes are elicited represents the receptive field of a particular nerve, allowing identification of the involved nerve or nerve root. Pain in the head and neck is mediated by the upper cervical spinal roots, the intermediate, glossopharingeal and vagus nerves, along with sensory fibers from the trigeminal nerve *(11)*.

Trigeminal neuralgia

The most common orofacial clinical entity involving underlying neuropathic pain is trigeminal neuralgia (TN). Trigeminal neuralgia; also known as *tic douloureux, Fothergill disease and suicide disease*; is estimated to

affect 4–13 people per 100,000 population *(11–13).* It occurs at a rate of about 15,000 new cases per year in the US (14). TN can occur at any age, including childhood, but the incidence generally increases with age. Idiopathic cases are the most common after the age of 50 *(15).* Considered a natural consequence of their longer life expectancies, women are about 1.5 times more likely to experience TN *(14).* Although the disease is more common in some families, 80–90% of TN is sporadic *(16)* and attributable to aberrant loop arteries or veins compressing the trigeminal root *(17–19).* This frequent etiology makes trigeminal neuralgia due to vascular compression *(10)* considered "classical" idiopathic trigeminal neuralgia. Secondary TN arises from compression by other structures, such as an acoustic neuroma, meningioma, epidermoid cyst, aneurysm or AV malformation *(10, 20–26).* Although all three branches of the trigeminal nerve may be involved, TN is usually limited to one or two branches. The second and third trigeminal branches are those most commonly affected by TN. The first branch of the trigeminal nerve is affected in only about 5% of TN cases, usually due to herpes zoster infection. The pain of trigeminal neuralgia is usually unilateral, sudden, severe, and sometimes described as lightning–like. Pain may be bilateral, but both sides are not usually affected at the same time *(14*). TN is often accompanied by paresthesias, such as burning and shock-like sensations. Pain and paresthesia symptoms can be provoked by chewing, talking, brushing teeth, cold air, laughing, light touch, smiling or any other stimulation of trigger-points around the nose and mouth. As is typical of allodynia, the pain induced by trigger-points is usually disproportionate to the stimulus, such that a mild stimulus causes severe pain. Notably, injection of local anesthetic at trigger-points is usually effective in providing pain relief. The pain of trigeminal neuralgia typically occurs as episodic attacks ranging in duration from a few seconds to several minutes. Whereas the pain typically subsides completely between episodes, some patients with long-standing TN experience pain continuously between paroxysms. Although the course of the disease is unpredictable, symptomatic periods of frequent TN paroxysms generally occur over the course of weeks or months, followed by periods of remission. The course of the disease for some patients tends toward unremitting pain while others experience a decrease in frequency and intensity of TN symptoms. Patients with trigeminal neuralgia are generally able to sleep through the night without suffering paroxysms of pain.

The diagnostic criteria for classical trigeminal neuralgia described in the Third International Classification of Headache Disorders (ICHD-3) of the International Headache Society (IHS) *(10)* are based on the timing, characteristics and distribution of OFP. Classic TN presents as paroxysmal pain that is intense, sharp, superficial, stabbing, or was precipitated from stimuli at trigger-points and lasts up to two minutes. The pain involves one or more branches of the trigeminal nerve and is not associated with any other disease. In addition, attacks are stereotyped in individual patients who have no clinically evident neurological deficit.

The ICHD-3 diagnostic criteria for secondary (or *symptomatic*) trigeminal neuralgia require that anything other than vascular compression causes the spectrum of symptoms associated with TN. One distinctive clinical feature of the secondary form is that it lacks a refractory period after paroxysms *(10).* Potential causes of secondary TN include acute herpes zoster, postherpetic neuralgia, trauma, multiple sclerosis plaques, and other non-vascular compressive lesions. Post-traumatic trigeminal neuropathy, or *anesthesia dolorosa*, is an important cause of secondary TN that is defined by the ICHD-3 *(10)* as one-sided pain of the face or oral cavity in a patient with a history of verified mechanical, chemical, thermal or radiation-induced trauma in the same area of the trigeminal nerve associate with symptoms. The pain must appear within three to six months after the traumatic event, and is not better characterized by another ICHD-3 diagnosis. The pain of post-traumatic TN must also be associated with clinically apparent positive or negative signs of trigeminal nerve dysfunction. Positive signs such as hyperalgesia and allodynia may coincide with negative signs such as hypoesthesia and hypoalgesia. The clinical finding of pain in a facial area where the sensation is either missing or impaired is characteristic of anesthesia dolorosa. Patients can find this mix of positive and negative symptoms difficult to explain, making a careful clinical history especially important in identifying causes of central pain such as post-traumatic TN.

While the precise mechanism remains to be fully elucidated, the symptoms associated with trigeminal neuralgia are likely due to demyelination in the area of compression or damage *(27, 28).* Demyelination also occurs in multiple sclerosis and other structural lesions of the brain stem, making these an important part of the differential diagnosis *(29–32).* Demyelinated areas can generate ectopic impulses that contribute to abnormal nerve conduction *(17).* Such alteration of afferent inputs can disinhibit pain pathways in the spinal trigeminal core. Evidence supporting involvement of central pain mechanisms includes the occurrence of a refractory period after triggered episodes of pain *(29).* During the refractory period, which usually lasts a few minutes, a paroxysm of pain is not possible. The complex mechanisms involved in the development and presentation of trigeminal neuralgia require a range of specialists including dentists and neurologists be included in a multidisciplinary approach to its diagnosis and treatment.

Herpes zoster and postherpetic neuralgia

Herpes zoster may cause pain with neuropathic characteristics in the area innervated by one of the facial

nerves. Systemic and topical analgesics may help but are usually insufficient for providing complete pain relief. The onset of pain from herpes zoster often precedes the occurrence of the vesicular rash and can persist even months after the lesions are no longer visible. The diagnosis of OFP due to herpes zoster is often difficult, particularly before the appearance of the characteristic rash. The primary factor confounding a clear diagnosis is that herpes zoster can mimic dental pain. Reliable laboratory tests for the unambiguous diagnosis of herpes zoster OFP have not yet been developed. Early diagnosis and treatment may help prevent the development of postherpetic neuralgia (PHN), a condition in which pain endures at least one month after the herpes zoster rash has healed. The pain is usually a continuation of that experienced before and during the acute herpes zoster skin eruption. While it usually lasts up to six months, PHN can continue for years after the rash has healed.

Atypical odontalgia

Atypical odontalgia is characterized by constant pain after removal of a tooth, tooth apex, or dental pulp. Also known as idiopathic, or *phantom*, toothache, this condition can also be caused by facial trauma. Studies have shown that atypical odontalgia appears in 3–6% of patients after endodontic treatment. In atypical odontalgia, a throbbing ache is experienced in the area of a tooth or alveolar process over prolonged periods. The sensation may be intermittent or constant, and persists despite a lack of clinical and radiographic evidence that would indicate a disorder related to the teeth. Patients may have difficulty localizing the pain, which is usually more intense on the side where the trauma or dental procedure occurred. The pain may spread into adjacent areas unilaterally and bilaterally, with the teeth most frequently affected being the upper premolars and molars. Local anesthesia can, but does not necessarily, alleviate the pain. Unfortunately, the symptoms of atypical odontalgia are often untreated as they are mistaken for a normal response to the treatment or trauma that precipitated this OFP condition.

Glossopharyngeal neuralgia

Glossopharyngeal neuralgia is an infrequent disorder that is likely due to compression of the glossopharyngeal or upper portions of the vagus nerve. Damage to these nerves is suggested by asymmetry in the movement of the soft palate and uvula or the absence of the emetic reflex *(33).* Glossopharyngeal neuralgia manifests as paroxysmal pain in the area innervated by the 9th and 10th cranial nerves and is most often experienced as pain in the throat, particularly when chewing and swallowing *(10, 34).* The pain, which is usually unilateral, can encompass the pharynx, base of the tongue, and the area inferior to the angle of the mandible and ear. The pain may encompass the receptive field of the auricular and pharyngeal branches of the vagus nerve. Bilateral involvement is possible and occurs in about 12% of patients *(35).* The carotid arteries should be examined for pathological changes such as arterial dissection, before considering other potential sources of pain in this region. If the teeth, ears and carotid arteries have been eliminated as the source of pain, glossopharyngeal neuralgia should be considered in the differential diagnosis. Trigeminal neuralgia, which is 70 to 100 times more common than glossopharyngeal neuralgia, can occur as a comorbid condition .

The pain of glossopharingeal neuralgia is usually projected from the oropharynx to the ear. It is usually paroxysmal and intense, but can be superimposed on a constant, less severe pain. Attacks may occur several times per day and may even arouse the patient from sleep. The ICHD-3 diagnostic criteria for glossopharyngeal neuralgia requires at least three attacks of unilateral pain, in the base of the tongue, tonsillar fossa, pharynx, below the angle of the mandible or ear in patients without evident neurological deficit *(10).* Glossopharyngeal neuralgia occurs in paroxysmal attacks of strong, sharp, stabbing, or throbbing pain that lasts up to two minutes. Movements such as swallowing, coughing, talking or yawning can induce paroxysms of pain. Such findings, if not better characterized another ICHD-3 diagnosis, confirm a diagnosis of glossopharyngeal neuralgia. As with trigeminal neuralgia, glossopharyngeal neuralgia exists as either a primary or a secondary OFP condition. Secondary glossopharyngeal neuralgia can be caused by demyelinating lesions, tumors in the cerebellopontine angle, peritonsillar abscess, aneurysm of the carotid artery, Eagle's syndrome, *(36–39)* and vascular compression of the vertebral artery or rear lower cerebellar artery. Similar to trigeminal neuralgia, episodes of glossopharyngeal neuralgia can last for weeks or months, punctuating long periods of remission. A key diagnostic feature, glossopharyngeal neuralgia is the only cranial neuralgia in which painful afferent impulses can precipitate a cardioinhibitory reflex causing vagal bradycardia, asystole and syncope *(34, 40).* This symptom must be distinguished from cardiac pain that radiates to the orofacial area, such as may occur with sickle cell anemia and some neoplasms. It should be noted that pain resembling that of glossopharyngeal neuralgia can also be of traumatic, postoperative, and psychogenic origin. Also included in the differential diagnosis of glossopharyngeal neuralgia are several rare disorders such as neuralgia of the intermediate nerve, occipital neuralgia, optic neuritis, headache due to ipsilateral ischemic lesions of the oculomotor nerves (III, IV and VI), Tolosa Hunt syndrome, Raeder's syndrome, recurrent painful ophthalmoplegic neuropathy, neuralgia of the superior laryngeal nerve, burning mouth syndrome, persistent facial pain, temporal arteritis and carotidynia. Although uncommon, glossopharyngeal neuralgia is an important consideration in the differential diagnosis of OFP.

Diagnostic approach to OFP

Multiple factors contribute to the diagnostic and therapeutic challenges related to orofacial pain, making a multidisciplinary approach essential to the treatment of this disorder. OFP may arise from a variety of tissues in the face and head, including the meninges, cornea, dental pulp, oral mucosa, nasal mucosa and temporomandibular joint. So, the many pathophysiological mechanisms giving rise to orofacial pain is reflective of the diverse tissue types in which it originates. A lack of validated diagnostic criteria is one of several obstacles to improving care for patients, but also in translational research. Although efforts have been made in the classification of patients with temporomandibular joint disorder *(41),* headache *(42)* and orofacial pain *(43),* clinical trials indicate that the results of pharmacological, electrophysiological and imaging studies have not yet provided sufficient means for the comprehensive diagnosis of orofacial pain *(44, 45).* Screening questionnaires, such as the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS), Neuropathic Pain Diagnostic Questionnaire (DN4), Neuropathic Pain Questionnaire (NPQ) and others, can help in the identification of neuropathic pain, but conclusive results require assessment of questionnaire findings in light of the clinical examination and other diagnostic methods. Despite its format, the optimal diagnostic tool should distinguish neuropathy from other OFP etiologies. Another factor potentially contributing to diagnostic and therapeutic failure is insufficient education about pain in medical education programs. Anecdotal evidence of such a shortcoming was recently confirmed in a study of 242 medical schools from 15 European countries. The authors found that 82% of medical programs do not include a separate, compulsory course on pain in the curriculum. In schools that do dedicate coursework specifically to the study of pain, students only receive an average of 12 elective or mandatory educational hours on pain management, equating to only 0.2% of the overall educational program *(46).* A similar proportion of medical education in the United States and Canada is dedicated to the management of pain conditions *(5).*

The development and management of analgesic therapies presents another area of future improvement. While there has been significant progress in the identification of pathophysiological mechanisms underlying acute and chronic pain, this knowledge has not led to the development of new analgesic or coanalgesics which are more efficient, safer or have fewer side effects. In the treatment of most chronic neuropathic pain conditions, opioid and non-steroidal anti-inflammatory drugs (NSAIDs) remain the therapies most frequently prescribed in clinical practice *(47).* The use of these drugs is very often limited because of the risk for abuse of opioids and the gastrointestinal, renal and cardiovascular side effects associated with NSAIDs *(48, 49).* Other therapies more specifically targeting neuropathic pain are included as the accepted standard of care in algorithms published by professional organizations. These include tricyclic antidepressants, serotonin reuptake inhibitors (SSRIs), selective serotonin norepinephrine reuptake inhibitors (SSNRI), anticonvulsants, topical lidocaine, topical capsaicin, intrathecal opioids, corticosteroids and ziconotide. This variety of therapies offers clinicians the potential to utilize drugs whose mechanisms of action more specifically targets the particular pathophysiological processes underlying a given pain condition. Most of these therapies act on specific neurotransmitters involved in pain pathways, providing a sound theoretical basis for their use in the treatment of neuropathic and nociceptive pain. Tramadol, for example, provides opioid-like activity and also modulates serotonergic and noradrenergic systems. Antidepressants also provide pain relief through the modulation of select neurotransmitters while also helping to alleviate symptoms of depression, a frequent comorbid condition for those suffering from chronic pain. Among the oldest drugs in this therapeutic group, tricyclic antidepressants (TCAs) appear to modulate pain by potentiating the antinociceptive roles of serotonin and norepinephrine. The activity of both of these neurotransmitters has been shown to be enhanced by the TCA amitriptyline, the drug most commonly used when an antidepressant is included in the treatment of chronic pain. The efficacy of newer antidepressants varies according to class. While SSRIs have been shown to be less effective than TCAs in treating neuropathic pain, SSNRIs are more effective being recommended as the drug of choice in some guidelines *(50).* If medication management fails, then surgical procedures may be considered, such as a microvascular decompression to remove pressure from the trigeminal or glossopharyngeal nerve, radiofrequency thermocoagulation, gamma knife radiosurgery, or rhizotomy *(51, 52).*

Potential barriers to proper pain treatment were underscored by the results of a recent study in Croatia. The cross-sectional controlled study was conducted on 100 patients with chronic neuropathic orofacial pain of non-odontogenic origin. The results confirmed previous findings that pain imparts a significant effect on quality of life as measured by standardized parameters *(53).* The study also revealed that the treatment of chronic neuropathic pain is not in accordance with recommendations from IASP, European Pain Federation EFIC or The Croatian Pain Society. The study found that 61% of patients used NSAIDs and another 34% of patients used the weak opioid tramadol alone or in a fixed combination with paracetamol. Only 20% of the study participants were receiving an anticonvulsant. Medicines from the group of strong opioids, tricyclic antidepressants, corticosteroids and spasmolytics were not used by any respondent. An insignificant number of patients reported using some other treatment, such as acupuncture or biofeedback. Some respondents were not receiving any ongoing therapies.

It can be concluded from this study that the majority of neuropathic pain treatments administered in Croatia are not in accordance with current guidelines. This may be largely explained by administrative restrictions on drug prescriptions. Physicians nationwide are largely guided in their choice of drug therapy by the extent to which specific medications are fully covered by the Croatian Health Insurance Fund.

CONCLUSION

The future of orofacial pain treatment depends on the development of several key areas. Firstly, further research is required to firmly establish a comprehensive, sensitive and specific diagnostic classification scheme for all types of orofacial pain. This tool should integrate quality of life indicators such that they provide additional data on clinical outcomes *(54).* Additionally, the curriculum of study for doctors of both medicine and dentistry should include an increased number of educational hours devoted specifically to the treatment of pain. Finally, health policy should be harmonized such that the guidelines for prescribing medications established by insurance providers match the most recent evidence-based recommendations for the treatment of neuropathic pain.

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Ultrasound use for nerve blocks and management strategies in outpatient surgery

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INTRODUCTION

Advances in surgical technique favoring minimally invasive approaches and economic pressure to reduce hospital costs have led to a worldwide increase in the number of surgeries performed on an ambulatory or day-case basis, with patients admitted to the hospital on the day of surgery and discharged several hours later.

That trend is most pronounced in the United States, where the majority of surgeries are being performed as day-cases and a similar trend is expected in surgical centers across Europe as well.

The challenge for the anesthesiologist is to provide anesthesia that will combine pain and stress-free surgery with rapid recovery and good postoperative pain control to enable the patient to be discharged from the hospital capable of self-care in a home environment. Anesthesia related factors including insufficient postoperative pain control, drowsiness and postoperative nausea and vomiting (PONV) have been identified to be among the main reasons for delayed discharge and unplanned readmission after ambulatory surgery *(1, 2)*.

Although ambulatory procedures are considered to be minor surgical interventions, a significant proportion of patients still experience moderate to severe pain after these procedures *(3),* especially after orthopedic surgery.

Regional anesthetic techniques have been shown to significantly reduce pain scores, postanesthesia care unit utilization, postoperative nausea and vomiting (PONV) and need for opioid rescue analgesia compared to general anesthesia in patients undergoing ambulatory surgery *(4)*. Although it is reasonable to assume this should translate into earlier home readiness and shorter total hospital stay, such an advantage has not been consistently demonstrated for regional anesthesia in the ambulatory setting.

Introduction of ultrasound guidance for peripheral nerve block performance and perineural catheter placement has led to a reduction in block performance time, volume of local anesthetic administered and less intravascular injections, and resulted in lower need for opioid rescue analgesia compared to neurostimulation guided techniques *(5, 6,7)* however reduced overall complication rates compared to traditional techniques could not be demonstrated *(8)*.

Ultrasound guidance is also used to facilitate the performance of blocking deeper lying neural structures (e.g. paravertebral blocks), however these procedures involve a greater risk of potentially serious complications such as pneumothorax or deep hematoma formation and the

benefit of their use in ambulatory patients should be carefully weighed against these risks *(9)*.

Orthopedic procedures involving upper and lower extremities are ideally suited to be performed using easy to learn regional procedures providing excellent operative anesthesia as well as postoperative analgesia.

GENERAL PRINCIPLES

Depending on type of surgery, patient and surgeon preference, regional nerve block techniques can be used as the sole anesthetic or can be combined with sedation or general anesthesia to improve patient comfort and procedure tolerance. If the later is the case, care should be taken to choose sedative/anesthetic drugs which will allow for rapid recovery of consciousness and carry a minimal risk of postoperative nausea and vomiting *(10)*. If airway patency maintenance is an issue a laryngeal mask airway device may be preferable to endotracheal tube placement since it does not require the administration of muscle relaxant agents and is better tolerated by the patient reducing or precluding the need for intraoperative opioid administration.

Regional blocks should be performed prior to the procedure even if combined with general anesthesia, since they have significant opioid sparing effects, enhancing patient recovery by reducing opioid related side effects such as PONV, respiratory depression and drowsiness.

Performance of regional anesthetic techniques has been associated with increased induction times compared to general anesthesia *(4)* and therefore if possible, to reduce operation room occupancy, should be performed outside the OR in a dedicated "block room" or in front of the OR while it is being prepared in between patients.

If postoperative neurologic assessment is an issue then a perineural catheter should be placed prior to the procedure and a bolus of short acting or dilute long acting local anesthetic used to cover the operative period and allow for quick block resolution thereafter. After return of motor and sensory function and postoperative neurologic evaluation is completed a bolus of long acting local anesthetic can be administered to provide prolonged postoperative analgesia and the catheter removed before discharge from hospital or the patient discharged home with a portable pump delivering a continuous infusion of local anesthetic solution.

There are different types of portable pumps that can be used in an ambulatory setting. Simple dispensable elastomeric pumps deliver a fixed rate of local anesthetic and are easy to use not requiring any special intervention by the patient after being set up. Using more complex programmable mechanical pumps the delivery rate of LA can be adjusted and boluses administered as needed according to variations in pain intensity and the need for mobilization and performance of daily activities. Pumps can be set up to allow re-programming by the patient with limits set to maximum infusion rate and number of boluses administered or can be remotely controlled by medical staff after being contacted by the patient. Besides theoretical advantages, there is no clear evidence to show superiority of re-programmable pumps over modern fixed rate delivery systems *(11, 12, 13)*.

The lowest concentration of local anesthetic providing satisfactory analgesia should be chosen for continuous infusion, ideally allowing for at least partial preservation of motor function (e.g. ropivacaine 0.2% or bupivacaine 0.0625%-0.125% at 6-8ml/hr for upper extremity blocks and 4-6 ml/h for lower extremity blocks).

If local organizational issues and safety concerns preclude the use of continuous regional techniques in ambulatory patients, single shot nerve block duration can be prolonged by the use of adjuvants such as dexamethasone.

Clear and easy to follow institutional protocols must exist for ambulatory patients discharged with a regional block in place. Motor and sensory function should be documented prior to block placement and at discharge and the patient receive verbal as well as written instructions on precautions necessary to protect the insensate body region. An immobilizing device as a simple sling or orthosis should be provided to prevent injuries to the upper extremity and crutches and/or locked orthosis to allow ambulation and weight bearing with an insensate or weakened lower limb.

If a perineural catheter is placed the patient should be instructed on proper care and how to remove it once the infusion runs out. Ideally the catheter should be removed by medical personnel and documented, however this may impose further organizational and economic burdens and a simple telephone interview to receive patient feedback may be sufficient and preserve cost-effectiveness and patient satisfaction *(14)*.

Regardless whether the patient is discharged with a single shot or continuous nerve block, clear instructions must be provided to manage breakthrough and pain after the block wears off. A multimodal oral regimen combining paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) or selective COX-2 inhibitors with tramadol for more severe pain is appropriate for the first 3-5 postoperative days. Ideally a basal oral regime of paracetamol should be started already at the hospital after an intraoperative intravenous "loading" dose. This may diminish discomfort related to the perineural catheter, which can itself be a source of mild pain, or relieve tenderness at the block performance site. NSAIDs may then be added towards the end of the expected block duration period to prevent or lessen rebound pain and tramadol or another oral opioid analgesic agent added in cases where more severe pain is expected.

UPPER EXTREMITY BLOCKS

Surgery of the entire upper extremity is particularly suited to be performed under regional anesthesia since all of its innervation is derived from a single neural structure – the brachial plexus, originating from the ventral rami of the 5th cervical to the 1st thoracic (C5 to Th1) nerve roots with minor contribution coming also from C4 and Th2.

Various approaches to the brachial plexus have been described using surface anatomical landmarks above and below the clavicle *(15).* The traditional approaches to the brachial plexus are the interscalene, supraclavicular, infraclavicular and axillary approach. Using ultrasound to directly visualize the components of the brachial plexus and surrounding structures has enabled anesthesiologist to be more flexible with their approach and tailor it according to the individual anatomy of the patient. It reduces block performance time, the number of needle passes and incidence of vascular puncture, shortens sensory block onset time and improves block success *(16).*

The space inbetween the fascia of the anterior and medial scalene muscles and covered by the prevertebral fascia contains the roots and trunks of the brachial plexus (Figure 1). Landmark techniques usually use the cricoid cartilage to mark the level of needle point entry lateral on the neck (C6 level). Blocking the plexus at this level has consistently produced excellent analgesia for shoulder surgery since it reliably blocks both the suprascapular and the axillary nerves, supplying the majority of sensory innervation to the shoulder joint. Traditonally up to 50ml of LA have been used for interscalene block. Ultrasound guidance has enabled precise deposition of LA immediately adjacent to individual nerve roots and/or trunks of the brachial plexus producing reliable blocks with much smaller volumes, thus decreasing concerns of local anesthetic systemic toxicity. A volume of 20ml of levobupivacaine will produce shoulder analgesia for 12-16 hours. Adding 8mg of dexamethasone to a long acting local anesthetic will increase block duration to nearly 24 hours *(17).* Interscalene block is linked to a high incidence of ipsilateral phrenic nerve block resulting in hemidiaphragmatic paralysis and therefore should be used with caution in respiratory compromised patients. Involvement of the recurrent laryngeal nerve is also a concern. The C8 and Th1 roots often remain spared by this block making it unsuitable for surgery involving the ulnar nerve distribution on the arm or hand.

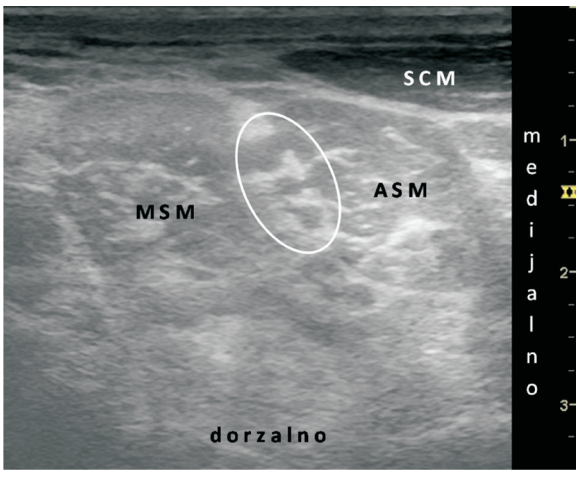

Figure 1. *Brachial plexus in the interscalene region. ASM – anterior scalene muscle; MSM – medial scalene muscle.*

Patients undergoing shoulder arthroscopy, rotator cuff repair and even arthroplasty have been successfully managed using interscalene brachial plexus blocks and consistently report less pain, lower opioid consumption and earlier commencement of passive range of motion exercises compared to those who received general anesthesia *(18).* Inserting a catheter for continuous LA infusion in the interscalene region can prolong analgesia in patients undergoing shoulder surgery and has successfully been used in ambulatory patients with no significant complications *(19).*

The trunks and divisions of the brachial plexus are tightly grouped together as they converge to pass above the first rib and below the clavicle adjacent to the subclavian artery, making this an ideal location to block the entire brachial plexus with a single injection. Prior to introduction of ultrasound guidance the supraclavicuar approach to the brachial plexus has fallen out of favor due to concerns of pneumothorax and a high risk of intravascular injection since the dorsoscapular artery often runs in between parts of the brachial plexus *(20).* With ultrasound guidance it is an excellent block for all surgical procedures on the upper extremity below the shoulder (Figure 2.). Due to its complete coverage of the brachial plexus it is also referred to as "the spinal of the arm".

The deeper position of the brachial plexus cords in the infraclavicular region may make ultrasound visualization more difficult compared to supraclavicular and axillary approaches, especially in obese or muscular patients. Injecting local anesthetic adjacent to the posterior cord decreases incomplete infraclavicular block rates due to ulnar nerve sparing. Due to easy catheter fixation and maintenance the infraclavicular approach is especially suitable for continuous analgesia after arm and hand surgery. Studies have demonstrated superiority of the infraclavicular approach to general anesthesia for day-case surgery in terms of postoperative pain control and patient satisfaction *(21, 22).*

The axillary block is the mainstay of regional anesthesia for elbow, forearm and hand surgery. It is a rather safe and easy to perform block. Due to its superficial location ultrasound provides excellent visualization of individual nerves surrounding the axillary artery and reduces the risk of vascular puncture. The musculocutaneous nerve

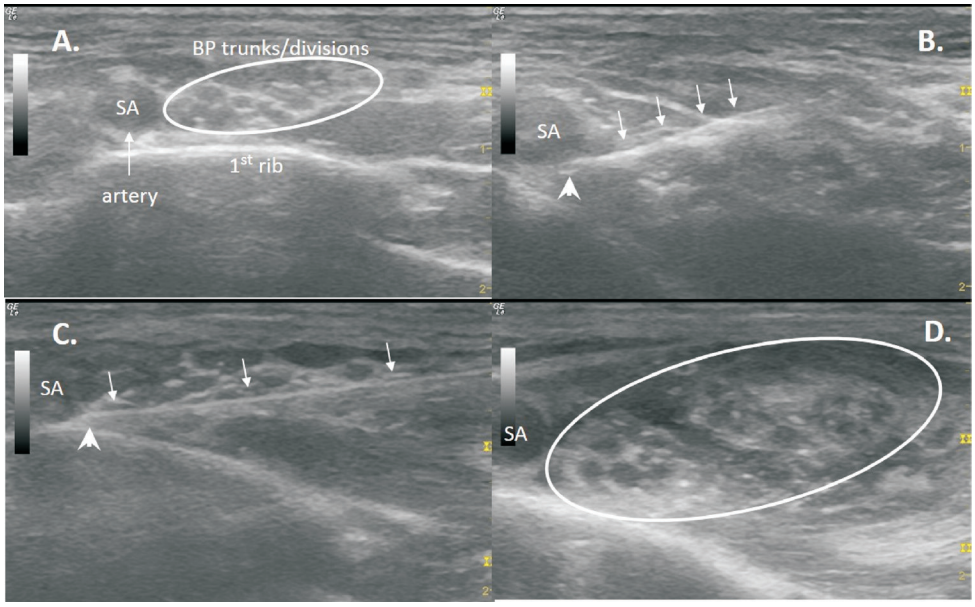

Figure 2. **A.** *Brachial plexus in the supraclavicular region.* **B.** *and* **C.** *In plane visualization of needle shaft (arrows) and tip (arrowhead) in "corner pocket" position.* **D.** *Trunks/divisions of the brachial plexus surrounded by local anesthetic. BP – brachial plexus; SA – subclavian artery.*

often separates high in the axilla from the rest of the brachial plexus and enters the coracobrachialis muscle often resulting in incomplete anesthesia and decreased tourniquet tolerance after paresthesia and neurostimulation guided techniques. Ultrasound guidance helps reliable identification and blockade of the musculocutaneus nerve at the axillary level.

Selective distal individual nerve blocks around the elbow are easily and quickly performed using direct visualization under ultrasound and can be used as the sole anesthetic for minor procedures on the wrist and forearm involving a single nerve teriotory or as "rescue" procedures following an incomplete proximal brachial plexus block.

Intravascular regional anesthesia (IVRA / Bier's block) has been a popular technique for below elbow procedures of short duration since it is simple to perform and has a high success rate. In short, IVRA is performed by exsanguinating a limb, applying a pneumatic tourniquet to cut off circulation and injecting local anesthetic into a vein distally on the limb. It provides good anesthesia for surgery involving soft tissue and superficial structures yet may be insufficient for procedures involving bone and articular structures. Drawbacks are risks of premature tourniquet deflation leading to systemic local anesthetic leakage, limiting it to short acting local anesthetics, poor tourniquet tolerance even with double chamber systems and negligible duration of postoperative analgesia. It can be used as a rescue procedure after incomplete brachial plexus and individual peripheral nerve blocks.

Local anesthetic infiltration can be used as the sole anesthetic for minor procedures on the wrist and hand or to supplement a regional block.

LOWER EXTREMITY BLOCKS

Lower extremity innervation is derived from the lumbar (anterior divisions of L1, L2, L3 and part of L4 spinal nerves) and sacral (L4, L5, S1, S2 and S3 spinal nerves) plexus.

Neuraxial anesthesia is the only way to provide anesthesia to the entire lower extremity via a single injection of local anesthetic. The advantages of spinal anesthesia for outpatient surgery are that it is simple, has a fast onset and low cost. Disadvantages include bilateral involvement, impaired ambulation, risk of urinary retention and fast onset of pain with block regression. Return of lower extremity motor function after spinal anesthesia is faster when short acting local anesthetics are used. Lidocaine has been a popular choice but its use has been discouraged after reports of a high incidence of transient neurologic symptoms *(23)*. Chloroprocaine is a short acting local anesthetic that has regained popularity for outpatient surgery in recent years. Block duration varies with the dose administered and roughly 40-60min of surgical anesthesia can be expected with a dose of 30mg, prolonged by about 15min with each additional 10mg increase in dose (*24*). Another strategy is to use low-doses of hyperbaric ropivacaine or bupivacaine solutions in an effort to achieve unilateral spread with patient positioning and decrease block duration. In a prospective randomized trial doses of 8 mg of hyperbaric bupivacaine 0.5%, 8 mg of hyperbaric levobupivacaine 0.5% or 12 mg of hyperbaric ropivacaine 0.5% resulted in similar discharge time for outpatient inguinal herniorrhapy *(25)*. Doses of 4-5mg hyperbaric bupivacaine produce effective spinal anesthesia for outpatient knee arthroscopy *(26)*.

The lumbar plexus gives rise to the genitofemoral, lateral femoral cutaneous, femoral and obturator nerves. Combination with a sciatic nerve block will result in complete lower extremity anesthesia and when performed with short-acting local anesthetics has been shown to be associated with a superior recovery profile compared with general anesthesia in patients having outpatient knee arthroscopy *(27)*.

Lumbar plexus or psoas compartment block is a deep block since the plexus is situated at a depth of 60-100mm within the psoas muscle anterior to the transverse processes of lumbar vertebrae *(28)*. When used in an outpatient setting it should be reserved for skilled operators and major procedures where its analgesic benefits outweigh the risk of potential complications. The peritoneal cavity, great vessels and kidney all lie anterior to the psoas muscle and can be penetrated with excessive needle advancement. Retroperitoneal and psoas muscle hematoma formation is also a potential complication of this block.

The femoral nerve is easily visualized by ultrasound as it emerges bellow the inguinal ligament into the upper thigh covered by the fascia lata and iliac fascia (Figure 3), the latter separating it from the femoral vessels. It always lies lateral to the femoral artery. Femoral nerve block produces anesthesia of the anterior thigh and knee and has been used to improve analgesia, facilitate early mobilization and reduce opioid consumption and related side-effects after complex outpatient arthroscopic knee procedures like anterior crutiate ligament repair *(29)* and arthroplasty. Quadriceps muscle weakness due to femoral nerve block impairs gait control and weight bearing and care must be taken to discharge the patient with adequate knee immobilization and crutches as well as written and verbal instructions how to prevent falls. To decrease quadriceps motor inhibition adductor canal nerve block targeting the saphenous nerve in the subsartorial mid-femoral region has become a popular option *(30)* although its analgesic benefit in outpatients undergoing ACL reconstruction has recently been questioned *(31)*.

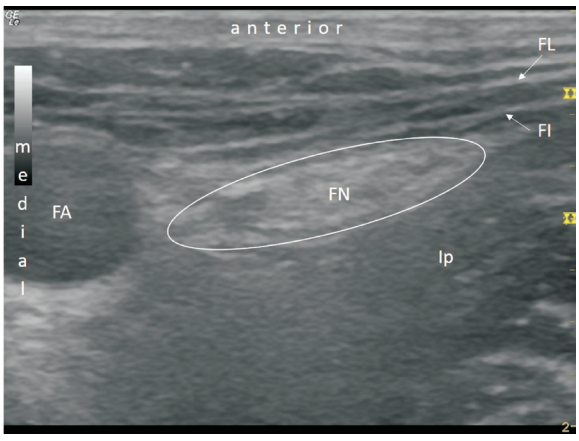

Figure 3 *Femoral nerve in inguinal region. FA – femoral artery; FI – fascia iliaca; FL – fascia lata; FN – femoral nerve; Ip – iliopsoas muscle*

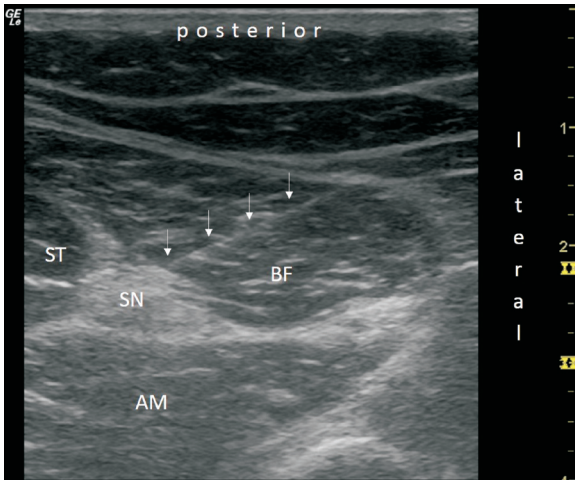

Figure 4 *Sciatic nerve in the upper thigh and in plane view of 26 gauge needle (arrows) AM – adductor magnus muscle; BF – biceps femoris; SN – sciatic nerve; ST – semitendinosus*

The sciatic nerve innervates the posterior thigh and almost the entire lower leg. Due to its deep location it is a technically demanding block when performed in the parasacral and gluteal region, however is readily visible with ultrasound from the subgluteal to popliteal region.

Proximal blocks of the sciatic nerve (Figure 4) are used to supplement lumbar plexus and femoral nerve blocks for surgeries performed on the thigh and knee, while blocking it at the popliteal region produces excellent anesthesia for most below the knee surgical procedures with the advantage of preserving hamstrings muscle strength and knee flexion. Sometimes a saphenous nerve block is added to improve calf tourniquet tolerance and provide complete anesthesia for surgeries involving the anteromedial portion of the lower leg. Continuous sciatic blocks provide good postoperative analgesia after day-case foot surgery without increasing complication and readmission rates compared to inpatients *(32)*.

Peripheral blockade of individual nerves around the ankle (ankle block) can be equally effective as a popliteal sciatic nerve block to provide both surgical anesthesia as well as postoperative analgesia after forefoot surgery *(33)*. It has the advantage of preserving lower leg motor function but requires multiple injections and does not cover the use of a calf tourniquet. Ultrasound guidance enables faster block performance and reduces the amount of local anesthetic lessening patient discomfort during block performance (Figures 5, 6).

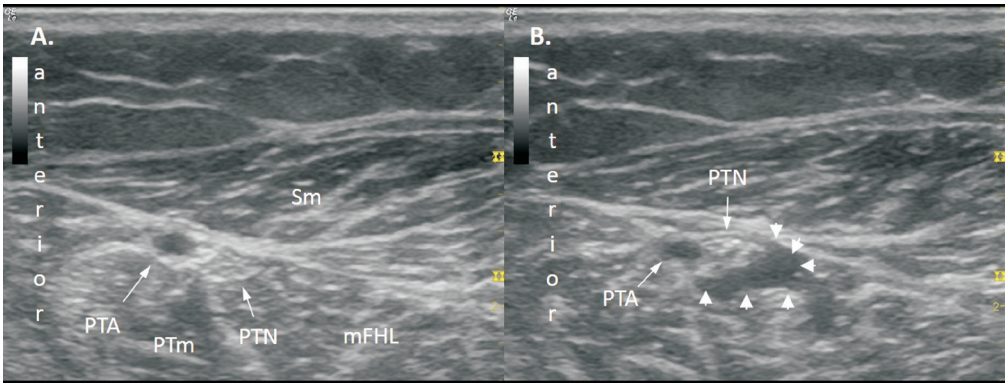

Figure 5. A. *Posterior tibial nerve and artery in the supramaleolar region* **B.** *Spread of local anesthetic (arrowheads). PTA – posterior tibial artery; PTN – posterior tibial nerve; PTm – posterior tibial muscle; mFHL – flexor hallucis longus muscle; Sm – soleus muscle.*

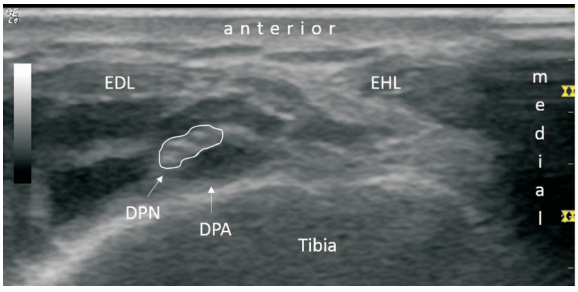

Figure 6. *Deep peroneal nerve at the level of the ankle. DPA – dorsalis pedis artery; DPN – deep peroneal nerve; EDL – extensor digitorum longus; EHL – extensor hallucis longus.*

TRUNCAL BLOCKS

The thoracic paravertebral space is situated between the vertebral body and intervertebral foramina medially, parietal pleura anterolaterally and superior costotransverse process dorsaly. Injection of local anesthetic into this space results in segmental anesthesia similar to an epidural block. Thoracic paravertebral blocks have been successfully used to reduce pain after breast surgery *(34),* minor and major thoracic surgery *(35)* and cholecystectomy *(36).* It has also been used for pain control after rib fracture management in an outpatient setting *(37).* A recent metaanalysis found PVB to be associated with less hypotension, PONV, urinary retention and failed block compared to epidural anesthesia *(38).* Nevertheles, paravertebral blocks have the potential for serious adverse effects, such as pneumothorax, vascular puncture and spread of local anesthetic into the epidural space. There is significant variability of spread of local anesthetic through the paravertebral space and sometimes injections at multiple levels may be necessary to achieve complete block of the surgical area. Injecting small volumes of local anesthetic at multiple levels may be a strategy to decrease the possibility of systemic toxicity as compared to achieve a greater segmental spread by injecting a greater volume at a single level. Inserting a catheter into the paravertebral space enables prolonged postoperative analgesia, however catheter dislogement and misplacement have occured relatively often prior to the introduction of ultrasound guided techniques *(39).* This technique should be reserved for skilled practitioners and its benefits carefully weighed against the risks in an outpatient population.

Transversus abdominis plane (TAP) block is achieved by administering local anesthetic into the fascial plane inbetween the internal oblique and transversus abdominis muscles producing unilateral segmental anesthesia of the abdominal wall. Ultrasound visualization has made this an easy to learn and easy to perform technique and safe alternative to paravertebral blocks to provide analgesia for surgical procedures in the periumbilical region and lower abdomen *(40).* TAP blocks performed in the subcostal area have been used to provide analgesia after cholecystectomy *(41),* however they have no effect on visceral pain- and a recent study found only marginal benefits in reducing pain while coughing and on reducing opioid requirements in patients undergoing laparoscopic day-case cholecystectomy *(42).*

CONCLUSION

Increased pressure to enhance patient turnover and decrease hospital length of stay, together with the advancement of surgical and anesthetic techniques has led to a significant increase in outpatient surgery.

The use of regional anesthesia techniques consistently leads to reduced opiate analgesic requirements and improved postoperative pain and patient satisfaction scores in surgical patients. It has been shown that it's use in patients undergoing outpatient surgery results in a decrease in post anesthesia care unit utilization and reduces costs.

The use of ultrasound guidance for peripheral nerve block performance has decreased block performance time, enables visualization of the target nerve(s) and sur-

rounding anatomy and real time imaging of needle path and local anesthetic spread leading to a decrease in local anesthetic volume and a lower incidence of accidental vascular puncture. Further studies are needed to show whether the wide spread use of ultrasound guided regional anesthesia will result in increased patient safety and shorter total hospital stay in patients undergoing surgical procedures on an outpatient basis.

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Scalp block for hemodynamic stability during neurosurgery

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Abstract

***Background and Purpose**: For elective neurosurgery procedures maintaining perioperative hemodynamic stability and optimal cerebral perfusion is of outmost importance. Beside numerous anesthetics techniques, risk of hemodynamic instability is still very high.*

***Materials and Methods**: We retrospectively analyzed perioperative values of heart rate and arterial blood pressure in 39 patients who underwent neurosurgery. We combined general anesthesia with scalp block. We blocked the supraorbital, supratrochlear, zygomaticotemporal, auriculotemporal, greater occipital, and lesser occipital nerves with 0,5% chirocaine, including 5 μg/mL of epinephrine that was performed after general anesthesia induction, before pin placement. Heart rate and blood pressure values were measured before anesthesia induction, after induction, after pins placement, after craniotomy and at the end of surgery. Changes of heart rate and blood pressure values less than 20% after painful stimuli was considered as a good hemodynamic stability of applied anesthetic technique.*

***Result:** Scalp block was successfully performed in all patients without complications. Measured values of heart rate and blood pressure before and after anesthesia induction compered to values after painful stimuli were within the 20% change.*

***Conclusion:** Scalp block, combined with general anesthesia provide good hemodynamic stability during neurosurgery.*

INTRODUCTION

For elective neurosurgery procedures maintaining perioperative hemodynamic stability and optimal cerebral perfusion is of outmost importance. Especially in patients with elevated intracranial pressure or scheduled for aneurysm repair. Although numerous anesthetics techniques are available the risk of hemodynamic instability at the very beginning of neurosurgical procedure during the placement of cranial pins of the head holder, craniotomy and dural incision is still very high *(1)*. Changes in blood pressure and heart rate could have adverse effect on patient cardiovascular system, intracranial pressure decreasing cerebral perfusion pressure and also could increase risk of aneurysm rupture *(2)*. One solution is high opioids techniques that could provide stress free anesthesia but has numerous drawbacks such as delayed emergence and incapability of early neurological evaluation after surgery. Combining regional anesthesia technique of scalp block just after induction of general anesthesia offers several advantages for most patients. Blocking the nerves that

sensory innervates crania helps to blunt the hemodynamic response to noxious stimuli stabilizing intraoperative hemodynamics, decrease the amount of opioids and decrease postoperative pain allowing smooth and fast emergence with lower incidence of chronic pain *(3)*.

Scalp block is easily performed by direct local anesthetics infiltration at the typical anatomical places and most proximal points where nerves that sensory innervate scalp and forehead (supraorbital nerve, the supratrochlear nerve, the zygomaticotemporal nerve, the auriculotemporal nerve, greater and lesser occipital nerves) emerges from scull *(1)*. Preferably long acting local anesthetics such as ropivacaine 0.75% or levobupivacaine 0.5% are used supplemented with 5 µcg/ml epinephrine for reducing systemic resorption and to elongate the duration of block *(4)*. Scalp blocks proved useful during awake craniotomy and for supplementation of general anesthesia for other forms of craniotomy *(1, 5)*.

Adverse effects of scalp block are rare and include unintentionally motor nerve infiltration with extension of the anesthesia to the motor nerves, unintentionally intravascular injection systemic toxicity and unintentionally intrarticular and intramuscular injection of the pterygoid muscles that can block temporomadibulary joint with limited oral opening and trismus *(1, 2)*.

MATERIAL AND METHODS

In observational study we retrospectively analyzed perioperative values of heart rate and arterial blood pressure in 39 patients who underwent neurosurgery procedure in whom we combined general anesthesia with scalp block. We included patients who underwent elective neurosurgery for intracranial mass lesion and aneurysm or AV fistula repair, ASA I to III. All patients preoperatively signed informed consent and agreed with scalp block procedure. Exclusion criteria were previously cardiovascular medication, including beta blocker or antihypertensive therapy with previously known local anesthetics allergy. After patients arrived in operating theater standard neuroanesthesiamonitoring were placed (ECG, invasive arterial blood pressure under local anesthesia, pulse oximetry) and peripheral intravenous line was introduced. All patients underwent same anesthetics technique. Anesthesia induction was done with fentanyl and propofol. Endotracheal intubation was facilitated with vecuronium. Scalp block was performed according to modern technique described in literature after anesthesia induction because of better patients' comfort *(1)*. We blocked six sensory nerves at the typical anatomical places where they emerge from skull with direct infiltration of local anesthetic.

Supraorbital nerve was blocked as it emerges from the orbit. After identification of supraorbital notch the needle was inserted along the upper orbital margin perpendicular to the skin 1 cm medial to the supraorbital foramen. Supratrochlear nerve was blocked as it emerges from the superiomedial angle of the orbit finger's breadth medial to supraorbital nerve.

Auriculotemporal nerve was blocked over zygomatic process 1 to1.5 cm anterior to the ear at the level of the tragus. Before injection superficial temporal artery was identified anterior to the auriculotemporal nerve at the level of the tragus to avoid intravascular injection.

The zygomaticotemporal nerve emerges from scull above zygoma between supraorbital and auriculotempoal nerves. Nerve was blocked with infiltration from the supraorbital margin to the posterior part of the zygomatic arch with deep and superficial injection of local anesthetics because of its ramifying. The greater occipital nerve was blocked by infiltration of local anesthetic 2.5 cm lateral to the nuchal median line, halfway between the occipital protuberance and the mastoid process. Lesser Occipital Nerve was blocked by infiltration along the superior nuchal line, 2.5 cm lateral to the greater occipital nerve block.

As a local anesthetic, we used 0,5% chirocaine with addition of with 5 µcg/ml epinephrine. During each infiltration 2–5 ml was injected with previously checking for unintentionally intravascular injection. For anesthesia maintenance we used TIVA technique with propofoland fentanyl. Anesthesia depth was monitored with entropy. Scalp block effectiveness was evaluated through maintained hemodynamic stability during painful stimuli of surgery (pinsplacement and craniotomy). Heart rate and blood pressure values were measured for five times: Before anesthesia induction (T1), immediately after anesthesia induction (T2), after scalp block (T3), after placement of head pins (T3) after craniotomy (T4) and at the end of operation (T5). Changes in heart rate and blood pressure values before painful stimuli (T1 and T2) of more than 20% in contrast to values after painful stimuli (T3 and T4) was considered as hemodynamic instability and inadequate scalp block effectiveness for analgesia during painful stimuli. Data are presented as average and median values in tables and figure.

RESULT

Demographic data are shown in table 1. In all patients planned scalp block was successfully performed after anesthesia induction and before painful stimuli. Average fentanyl dose during surgery was 0, 21 mg. Scalp block 0,5% chirocaine dose was 20 ml in all patients. In all patients measured values of heart rate and blood pressure before (T1) and after (T2) anesthesia induction compered to values after painful stimuli (T3 and T4) were almost the same with minimal variation that not exceed 20% change (Table 2 , Figure 1). There were no complications associated with scalp block in any patients.

TABLE 1
Demographic data.

Patients number	39
Female	21
Male	18
Age (years)	46
Intracranial mass lesion	30
Vascular pathology	9

TABLE 2
Average (median) values of heart rate and arterial blood pressure.

Measurement	Heart rate (beats/min)	Blood pressure (mmHg)
T1 before anesthesia induction	70 (75)	124/68 (125/65)
T2 after anesthesia induction	68 (65)	123/68 (130/63)
T3 after pins placement	66 (68)	124/67 (110/65)
T4 after carniotomy	66 (68)	121/67 (113/65)
T5 at the end of surgery	67 (68)	119/67 (1110755)

DISCUSSION

Optimal neuroanesthesia technique for craniotomy should enabled intraoperative hemodynamic stability with good perioperative pain control to avoid acute or chronic postcraniotomy headache. The main cause of pain arises from the insertion of scull pins into the periosteum and craniotomy. Systemic application of opioids could blunt the stress responsebut used in high dose couldhave adverse effect of lowering blood pressure and delayed emergence *(2)*. Regional anesthesia techniques, as a supplement to general anesthesia, could offer advantages such as lower stress response, better hemodynamic stability and lower postoperative pain *(3, 5)*. Most commonly used is scalp block and local infiltration of local anesthetic at the wound and the site of pins insertion. Several papers have described the use of scalp block to limit the neuroendocrine and hemodynamic response *(2)*. Cardiovascular stability as well as pain control has shown positive findings in outcome of neurosurgical patients *(2, 4)*. In our study, we follow the systolic and diastolic blood pressure, heart rate and consumption of opioid in patients that underwent craniotomy in general anesthesia with scalp block. Scalp block is sensory blockade of scalp and forehead. According literature, scalp block is effective, simple to use, easy to learn, with known but rare side-effects *(1, 3)*. Various local anesthetics such as lidocaine, bupivacaine, ropivacaine, with or without adrenaline, could be used. Papers reports application of block preoperatively or postoperatively after wound closure *(1, 3, 5)*. Moderate to severe postcraniotomy pain is present in more than 50% of patient after craniotomy *(5)*. According meta-analysis from 2013, scull block is associated with reduced postoperative pain in the first 12 hours and also reduced requirements of analgetics in the first 24 hours *(3)*. On the other hand, use of analgetics in the neurosurgery is limited by their side effects. Guilfoyle et al discuss the advantages of blocks over the use of opioids (nausea, vomiting) and NSAID (often parallel use of steroids) *(3)*. They conclude that poor treatment of postoperative pain in neurosurgery patients can be overcome with scalp blocks.Local wound infiltration is another alternative to scalp block. Geze et al carried out prospective, randomized, placebo-controlled study (2). Authors compared scalp block, infiltration block, and routine anesthesia in craniotomy on hemodynamic (mean arterial pressure, heart rate) and stress response (cortisol and adrenocorticotropic hormone). They reported that scalp block had better results compared to local infiltration of each skull-pin insertion point or routine anesthesia *(2)*. It is easy to explain because scalp block provide much superior sensoryblockade of scalp and forehead while local wound infiltration provide only short lived analgesia of wound area. Our data showed excellent hemodynamic stability in all patients with combined regional anesthesia scalp block and general anesthesia. Almost identical measured values of heartrate and blood pressure could be explained with carefully titrated anesthetics dose with TIVA, selected group of patients withoutsignificant cardiovascular morbidity and excellent suppression of painful stimuli of pins placement and craniotomy with previously done scalp block thatblunt stressresponse. These results were found

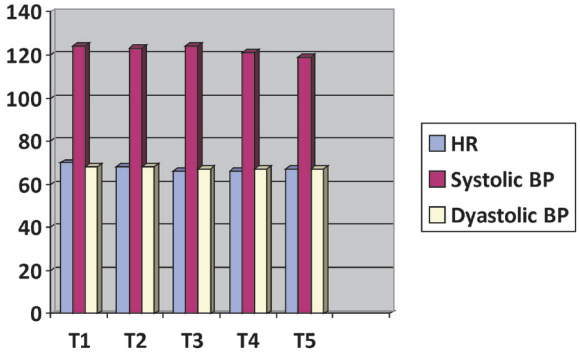

Figure 1. *Average heart rate (HR), systolic and diastolic blood pressure (BP) values.*

to be consistent with the results of other studies. In our study *(2, 4)* there were no complications associated with the block. According different authors, side effects of scalp block are rare *(1, 5)*. The main problem can result from the fact that local anesthetics should be given in relatively high amount in very vascularized area. Thus, it cannot beemphasize enoughthe importance of carefully administration of local anesthetics, and caution about maximum doses. Our study also has several potential limitations. First, the small sample size with only descriptive comparison of results, but it was conceived as pilot study and it should be confirmed on larger number of patients with proper statistical analysis. Second, biological different sensation of pain among patients could influence measured values so in the future studies some preoperative evaluation of pain potency sensation could be appropriate.. And third, because of small group of patients, incidence of complication can be under-recognized. In conclusion, in our study scull block as adjunct to general anesthesia provided neurosurgical patients with excellent hemodynamic stability. Dose of 20 ml of chirocaine for blockade of sensory cranial nerves was required for adequate scalp block. With regular precautionary measures throughoutthe blockadministration, scalp block was safe for patients, Scalp block prior painful stimuli, combined with general anesthesia, and couldbe anesthesia technique of choice for maintaining optimal perioperative hemodynamic in neurosurgery.

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Lumbar spinal stenosis: methods of treatment with emphasis on epidural steroid injections

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Key words: low back pain, spinal stenosis, epidural analgesia, steroids, chronic pain

Abbreviations (in alphabetical order):
CT = computed tomography
ESI = epidural steroid injection
LSS = lumbar spinal stenosis
MRI = magnetic resonance imaging
NSAID = nonsteroidal antiinflamatory drugs
RTG = X-ray radiation
VAS = visual analogue scale

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Abstract

Background and Purpose: *The aim of the study was to compare two techniques of steroid application into epidural space to patients with lumbar spinal stenosis (LSS), a chronic degenerative spine disorder.*

Patients and Methods*: Sixty LSS patients have been distributed into 2 groups: "BLIND" (n=30, interlaminar epidural steroid injection without RTG control) and "RTG" (n=30, transforaminal epidural injection with RTG control). All patients have received 80 mg of triamcinolon (Kenalog) into epidural space on L4/L5 level, together with 0,5% lidocain (patients in RTG group 3 ml and those in BLIND group 10 ml) in 3 week intervals. They were asked to describe the pain using visual analogue scales (VAS) at the beginning of treatment (VAS-0), after the first (VAS-1), the second (VAS-2) and the third epidural injection (VAS-3). The differences between groups were shown using t-test (age) and χ^2-test (gender). Medians of VAS scores were statistically described using non parametrial methods. P<0.05 was considered as a statistically significant.*

Results: *There is no statistical difference among patients regarding to age (P=0.93), gender (P=0.12) and VAS-0 score before the first injection (P=0.27). There is a statistically significant reduction of pain in relation to VAS-0 in both groups (P<0.001). Both groups do not statistically differ when it comes to their effectiveness in regards to VAS scores .*

Conclusions: *We did not find any statistical difference in postinterventional VAS scores among two groups of patients. Choice of technique depends on the experience of the anesthesiologist, as well as on the local technical possibilities (availibility of RTG devices).*

INTRODUCTION

Lumbar spinal stenosis (LSS) is a chronic, degenerative spine disorder and most common reason for pain and disability among people older than 60 years of age *(1).*

LSS can be a result of degenerative changes that result in neural ischemia and neurogenic claudication, a typical syimptom that is described as a pain in the gluteus with irradiation into both legs, usually reaches knees; weekness, parasthesia. The pain is most often felt while walking, standing for longer periods and walking downhill. All these changes significantly decrease the quality of life *(2).*

LSS is a result of degenerative spinal cascade, hence the stenosis has effects on central canal and nerve root canals as well (Fig.1). It is believed that neurogenic claudication is a result of structural narrowing of central

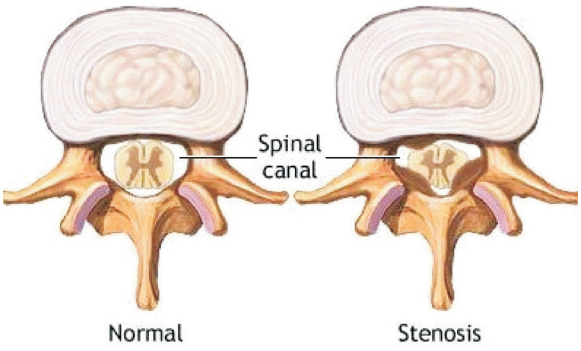

Figure: 1.

spinal canal, which impeds the venous return, thus causing venous hypertension and arterial ischemia of cauda equina *(3).*

The pain is decreased when leaning forward and over a supporting object (pushing a shopping trolley or walking with the aid of walkers). Since more areas are involved, patients suffering from LSS can have unilateral, bilateral, monoradicular or poliradicular symptoms *(4).*

Pathogenesis

LSS pathogenesis depends on multiple factors. There are vascular, biochemical and biomechanical factors that contribute to the signs and symptoms of LSS (3).

Diagnosis

Patients`history of illness states pain in glutei with irradiation into both legs, usually above and at the level of knees, weekness, parasthesia that increases while standing and walking.

The patients are at ease when flexing the spine. Computed tomography (CT) scans and magnetic resonance imaging (MRI) confirm the diagnosis.

Because of the involvement of more areas, patients with LSS can have unilateral, bilateral, monoradicular or poliradicular symptoms *(5).*

Treatment of degenerative lumbar stenosis

Conservative

- Adjusting activities
- Walking aids (walkers)
- Drugs (Paracetamol, nonsteroidal antiinflamatory drugs, low doses of opioids)
- Physical therapy and exercises

Interventional

- Epidural steroid injections
- Surgery

Conservative treatment is used early in the course of illness and among patients with mild to moderate symptoms. Multidisciplinary treatment is necessary and should involve physical therapy, wellness, smoking cessation and weight loss, if needed *(6,7).*

Pharmacological treatment

The first choice are nonsteroidal antiinflamatory drugs (NSAID). Opioid analgetics undoubtedly decrease pain, but are still controversal as a treatment of spinal stenosis *(8).* There is not sufficient evidence that joint use of gabapentin and physical therapy decreases pain and improves walking distance *(9).* Moreover, there is not enough evidence for usage of muscle relaxants, prostaglandin and calcitonin.

Surgical treatments are used after all other options have failed and in patients that experience moderate to severe symptoms *(10, 11).*

When it comes to interventional methods, epidural steroid injections (ESI) are one of the most common used methods in treatment of chronic pain in lowerback and legs *(6, 12, 13).*

There are 3 most often used approaches when injecting steroids.

- interlaminar (blind method)
- caudal
- Ttransforaminal (controlled with RTG)

Transforaminal approach implies the use of RTG in order to reach the nerve root. That is why a smaller amount of drug can be used and that makes it superior to the two therapy approaches. However, the chances for nerve damage with this approach are significantly higher *(6, 14).*

The effectiveness of injecting steroids into epidural space of patients with LSS is wellknown. However, there are not so many papers that compare the difference between both techniques when it comes to pain relief. The aim of this retrospective study is to show the difference between transforaminal and interlaminar epidural steroids injections and theire efect on pain reduction.

PATIENT AND METHODS

Sixty patients with LSS have been distributed into 2 groups: "BLIND"(n=30, interlaminar epidural steroid injection without RTG control) and "RTG" (n=30, transforaminal epidural injection with RTG control).Patients in both groups have received 80 mg of triamcinolon (Kenalog) into epidural space on L4/L5 level, together with 0,5% lidocain (patients in RTG group 3 ml and those in BLIND group10 ml). Patients from both groups received epidural steroid injections in 3 week intervals. They were asked to describe the pain using visual analogue scales (VAS) at the beginning of treatment (VAS-0),

after the first (VAS-1), the second (VAS-2) and the third epidural injection (VAS-3).The differences between groups were shown usingt-test (age) i $\chi 2$-test (gender). Medians of VAS scores were statistically described using non parametrial methods. P<0.05 was considered as a statistically significant.

RESULTS

There is no statistical difference among patients when it comes to age (P=0.93), gender (P=0.12) and VAS-0 score before the first injection(P=0.27). There is a statistically significant reduction of pain in relation to VAS-0 in both groups (P<0.001). Both groups, "BLIND" and "RTG", do not statistically differ when it comes to their effectiveness in regards to VAS scores (Table 1).

TABLE 1

VAS scores after the epidural steroides injections (Mann-Whitney U test).

VAS median, (1. i 3. kvartila)	Group BLIND (N=30)	Group RTG N=30	P
VAS-0	8 (7, 9)	7.5 (7, 9)	.266
VAS-1	6 (5, 6)	5 (4, 6)	.072
VAS-2	5 (4, 6)	4 (4, 5.25)	.098
VAS-3	4 (3, 5)	4 (3, 4)	.085

CONCLUSION

We did not find any statistical difference in postinterventional VAS scores among patients with LSS who received interlaminal (»BLIND») and transforaminal ("RTG") epidural steroid injections. Even though this research was conducted with a small number of participants, we conclude that the choice of technique depends on the experience of the anesthesiologist, as well as on the local technical possibilities (availibility of RTG devices).

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Radiofrequency denervation of lumbar facet joints in the treatment of chronic low back pain

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Abstract

Low back pain is the most common pain syndrome and a global health burden. The etiology in most cases is multifactorial and the facet joints can be a source of low back pain. The facet joint is innervated by the medial branch of the dorsal ramus of the spinal nerve. Facet joint disturbances can be responsible for 10% to 50% of all cases of chronic lumbar pain. In the absence of predictive clinical or radiologic findings, nerve blocks are considered to be the best way of diagnosing presumed facet-mediated pain. Radiofrequency ablation to induce thermal necrosis of the facet neural fibers has been reported to provide significant pain reduction in patients for 6–12 months. A radiofrequency neurotomy is a type of injection procedure used to treat facet joint pain caused by arthritis or other degenerative changes, or from an injury. In this procedure, a heat lesion is created on certain nerves with the goal of interrupting the pain signals to the brain, thus eliminating pain. Medial Branch Neurotomy could be considered an option for patients suffering persistent axial and referred non-radicular leg pain unresponsive to less invasive conservative measures.

INTRODUCTION

Low back pain is the most common pain syndrome and a global health burden. The etiology in most cases is multifactorial and the facet joints can be a source of low back pain. As first described by Goldtwaith in 1911 the facet joints can be a source of low back pain *(1).* The facet joint is part of the motion segment and consists of two articular surfaces, which are orientated almost vertically in the lumbar spine. Both the synovial folds and the capsule contain nociceptive nerve endings. The facet joint is innervated by the medial branch of the dorsal ramus of the spinal nerve *(2).* Each facet joint receives nerve endings from two heights. For example the facet joint L4–L5 receives nerve endings from the dorsal ramus from the 4th spinal nerve for the upper parts und from the 5th spinal nerve from the lower parts *(3).* The contribution of facet joints to low back pain is thought to linked to intervertebral disc degeneration in the concept of 'segmental instability'. As with degenerative changes the height of the intervertebral disc lowers there is more stress on the facet joints and the joint capsule with occurring osteoarthritic changes of the facet joint and possible pain generation *(4).* As degenerative changes occur in almost every person, facet joint osteoarthritis can be found in about 90% of all patients older than 50 years, but like in other locations there is little correlation between the extent of osteoarthritic changes and perceived grief *(5).* Between 8% and 12% of all patients with lumbar pain comprise chronic cases, with complaints last-

Figure 1. *Radiofrequency denervation in the operating room under the control of fluoroscopy and with the monitoring of patients.*

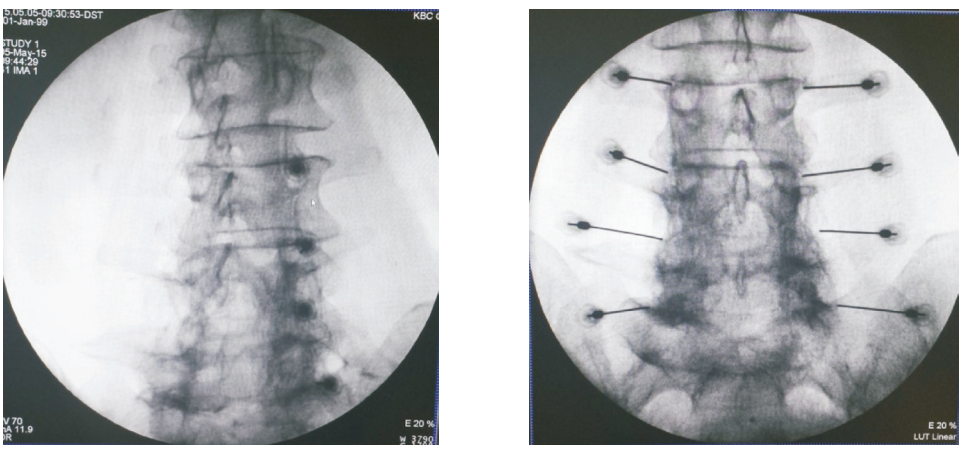
ing longer than three months *(6, 7)*. Facet joint disturbances can be responsible for 10% to 50% of all cases of chronic lumbar pain *(8–11)*. However, clinical history or physical examination cannot identify facet joint alterations as the origin of pain nor does imaging (e.g., radiography, computed tomography or magnetic resonance imaging *(12–20)*. In the absence of predictive clinical or radiologic findings, nerve blocks are considered to be the best way of diagnosing presumed facet-mediated pain *(21–25)*. Diagnostic blocks remain the mainstay in the diagnosis of facet joint syndrome and are used in most studies, even if they are questioned because of their sensitivity and specifity *(26, 27)*. A resolution or improvement of pain after image guided injection of local anesthetics around the joint capsule corresponding to the presumed time of action of the used local anesthetic makes the involvement of the facet joint probably (Figure 1).

In patients with unspecific chronic low back pain and unsuccessful conservative therapy (non steroidal anti-inflammatory drugs, physiotherapy) involvement of the facet joint should be considered and confirmed or ruled out with diagnostic blocks (Figure 2). Controlled diagnostic blocks imply having a patient undergo 2 separate injections, at different times, using anesthetic agents of different durations of action.

A positive response occurs when a threshold of pain relief (usually between 50–80%) is experienced and the duration of relief is consistent with the known duration of the anesthetic. Single diagnostic blocks use only a single injection and anesthetic agent.The only tool to identify facet joint alterations as the cause of pain is the verification of an analgesic response to anesthetic injections into the zygapophyseal joints or at their nerve supplies and medial dorsal branch blocks are easier to perform *(28–30)*. The diagnostic power of the blockade is based on the assumption that anesthetizing the facet joint or the capsule containing the innervations would result in pain relief. A positive result (i.e., pain relief) would mean that the facet joint is the site from which the pain originates. The technique of medial dorsal branch block consists of blocking each of the medial branches that innervate a facet above and a facet below their corresponding roots and also blocking the multifidus and interspinous muscles in the region of the corresponding dermatome *(27, 28)*.

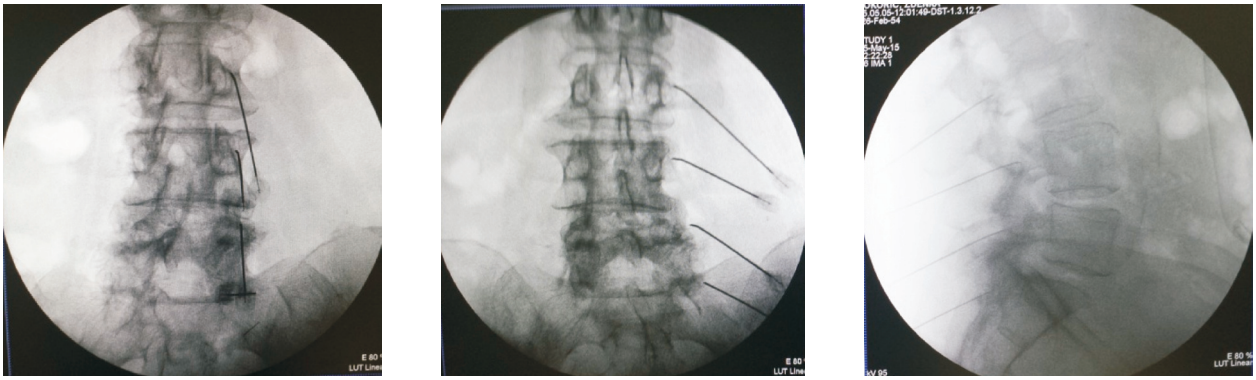
DISCUSSION

Radiofrequency ablation to induce thermal necrosis of the facet neural fibers has been reported to provide significant pain reduction in patients for 6–12 months *(28, 29)*. Radiofrequency facet joint denervation procedures have been common practice for 2 decades in treatment of chronic low back pain. A radiofrequency neurotomy is a type of injection procedure used to treat facet joint pain caused by arthritis or other degenerative changes, or from an injury. In this procedure, a heat lesion is created on certain nerves with the goal of interrupting the pain sig-



A B

Figure 2. **A.** *Oblique radiograph of the lumbar spine during lumbar medial branch block;* **B.** *Anterior-Posterior radiograph of the lumbar spine during lumbar medial branch block.*



A B C

Figure 3. A. *Oblique view demonstrating placement of radiofrequency cannulae after contact with "eye" of Scotty dog and slipped off the superior margin of the transferse processes;* **B.** *Anterior-Posterior radiograph of the lumbar spine during lumbar radiofrequency treatment of the lumbar facet jointsview of placet radiofrequency canulae,* **C.** *Lateral view of placement RF cannulae along the lumbar superior articular processes.*

nals to the brain, thus eliminating pain. The terms radiofrequency ablation and radiofrequency neurotomy are used interchangeably (Figure 3).

Both terms refer to a procedure that destroys the functionality of the nerve using radiofrequency energy. Success rates vary, but typically about 30% to 50% of patients undergoing this procedure for low back pain will experience significant pain relief for as much as two years. Of the remaining low back pain patients, about 50% will get some pain relief for a shorter period. As a general rule, if effective, the ablation will often provide pain relief lasting at least 9 to 14 months and sometimes for longer. After this period of time, however, the nerve will regenerate and the pain may return. Radiofrequency denervation showed efficacy in open as well as in placebo- controlled trials and could be a treatment option in carefully selected patients *(30).* After positive diagnostic blocks, denervation or therapeutic blocks with long acting local anesthetics and corticoids should be tried *(31).* Although medial branch neurotomy may benefit properly selected patients, the relief achieved is rarely complete or permanent. Because of this, treatment decisions are best based upon having a realistic understanding of expected outcomes in relation to a patient's current level of pain and physical function. Candidates for radiofrequency facet denervation should meet all of the following criteria:

- **No prior spinal fusion surgery in the vertebral level being treated;**
- Low back (lumbosacral) or neck (cervical) pain, suggestive of facet joint origin as evidenced by absence of nerve root compression as documented in the medical record on history, physical and radiographic evaluations; and the pain is not radicular;
- Pain has failed to respond to three months of conservative management which may consist of therapies such as nonsteroidal anti-inflammatory medications, acetaminophen, manipulation, physical therapy, and a home exercise program;
- A trial of controlled diagnostic medial branch blocks (2 separate positive blocks or placebo controlled series of blocks) under fluoroscopic guidance has resulted in at least a 50% reduction in pain; and
- If there has been a prior successful radiofrequency denervation, a minimum time of six months has elapsed since prior radiofrequency treatment (per side, per anatomical level of the spine).

Radiofrequency facet joint denervation is performed as a day procedure. All patients are given intravenous sedation to ensure they are as comfortable as possible throughout the procedure. The doctor performing the procedure will use local anaesthetic to numb patient skin before accurately inserting a needle using x-ray guidance next to the medial branch nerve to the facet joint. The doctor will then check that the needle is properly positioned by stimulating the nerve. This may cause muscle twitching and provoke some of pain. Once the needle is in the correct position, the area will be numbed and radiofrequency energy used to disrupt the medial branch nerve. Several nerves may need to be treated to obtain optimal pain relief. Patient will be monitored for 1–2 hours following the procedure prior to discharge. Full pain relief from the procedure may take several weeks. Most patients are able to return to work within two days following the procedure. Nerves regenerate after radiofrequency facet joint denervation. This usually takes between six months and two years. Dreyfuss et al followed 15 patients showing >80% relief on controlled diagnostic blocks. 13 had relief of >60% at one year, with 9 of these exceeding 90% pain reduction *(22).* Lakemeir et al assessed the 6-month response to medial branch neurotomy in 29 patients after showing a minimum of 50% pain relief to a single diagnostic block. Average pain scale re-

duced from 6.6 to 4.7. Oswestry Index reduced from 40.8 to 28. This study also compared facet denervation to intra-articular steroid injection, finding no statistical difference between the two procedures *(32).* The response to radiofrequency rhizotomy, after having successful comparative nerve blocks, in Goldfeld et al's study of 174 patients showed 119 having good (50%) to excellent (80%) pain relief and 55 showing no improvment. 96% of those with good-excellent responses had relief lasting between 6–24 months with 43% of that cohort showing sustained benefit for 2 years *(38).* Cohen *et al.* followed 262 patients who had a positive controlled diagnostic block with >50% pain relief. Following medial branch neurotomy, 54% had pain relief >50% lasting at least 6 months. There was no difference in response between those reporting >80% relief on confirmatory blocks as compared to those reporting relief of between 50–80% *(33).* A later study of his reinforced this finding, further concluding that the use of more stringent diagnostic criteria (higher pain relief thresholds or double as compared to single blocks) would likely result in withholding a beneficial procedure from a substantial number of patients without a corresponding improvement in success rates. Not all studies have shown favorable results for Medial Branch Neurotomy. One of the largest double blind randomized trials found no difference in pain scores, physical function, or medication use between active intervention and sham groups *(34).* As briefly discussed earlier, even when Medial Branch Neurotomy is successful, relief is rarely complete or permanent. Smuck et al reviewed 16 articles finding that the average duration of >50% pain relief for an initial procedure was 9 months. Repeat Medial Branch Neurotomy carried a success rate between 33–85% with an average duration lasting 11.6 months *(35).* These statistics were similar to an earlier study also showing a 10-month average duration of benefit for both initial and repeat procedures *(36).* In general, a reasonable number of patients with > 50% pain relief on controlled diagnostic blocks (and possibly even a single diagnostic block) could expect to experience similar relief with medial branch neurotomy for an average duration of 6–12 months. Repeat medial branch neurotomy tends to yield similar results. Complication rates with Medial Branch Neurotomy are considered to be low, minor, and in most cases, transient. As with most procedures, there is a remote risk of bleeding, infection, nerve injury or allergic reaction to the medications used. In addition, the injections may cause some temporary soreness in back. However. complications from these techniques may occur. These include discomfort around the injection site, numbness of the skin, neuritis, pain from muscle spasm at injection site, permanent nerve pain and reactions to administered medications *(36).* Kormick et al had performed 2 studies involving a total of 741 denervations. These revealed 5 cases of neuritic pain lasting longer than 2 weeks, 5 cases of muscle soreness lasting less than 2 weeks, one case of prolonged muscle spasm, and no instances of motor deficits, sensory deficits, or infections *(37–39).* In summary, Medial Branch Neurotomy could be considered an option for patients suffering persistent axial and referred non-radicular leg pain unresponsive to less invasive conservative measures.

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Temporomandibular joint disorder and headache – one-year-follow-up

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Abbreviations:
DC/TMD – diagnostic criteria/temporomandibular disorders
DD – disc displacement
MFA – manual functional analysis
MRI – magnetic resonance imaging
TMJ – temporomandibular joint
VAS – visual –analogue scale

Key words: temporomandibular joint, magnetic resonance imaging, headache, osteoarthritis

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Abstract

Background and Purpose: *Aim of this study was to compare the clinical characteristics of patients from the subgroup with osteoarthritis (G-1) and patients with disc displacement (DD) (G-2) of TMJ related types of headaches and with one-year-follow-up after treatment.*

Patients: *G-1 included 70 patients who were treated for signs and symptoms of OA of TMJ. Pain intensity (at first examination T0) in TMJ was shown on the visual-analogue scale (0, no pain; 10, the worst pain) as well as headaches. They were treated by an occlusal splint and/or physical therapy with a six-month(T1) and one-year (T2) follow-up. G-2 included 35 patients from a subgroup with DD. Definitive TMJ-diagnoses were confirmed by magnetic resonance imaging.*

Results: *There was a significant age difference ($p<0.001$) between the two subgroups of TMJ diagnoses, however there were no differences in pain during the follow-up period. In the beginning, the pain amounted to T0: G-1 6.5 / G-2 6.1 and at T2: G-1 1.6 / G-2 1.7. The applied treatment modalities at T1/T2 achieved TMJs without pain in 27.14%/64.29% of patients from G-1 and in 28.57%/57.15% of patients from G-2. There were equal shares of patients without headache (G-1 54.3%; G-2 48 %). The share of tension headaches was G-1 10%, G-2 11.4%, migraines G-1 15.2%, G-2 22.9%, TMJ-related headache G-1 4.3%, G-2 11.4% and cervicogenic headache G-1 15.7%, G-2 5.7%.*

Conclusions: *Pain intensity and treatment success do not vary within the observed groups. Migraine and TMJ-related headaches are more common in patients from G-2.*

INTRODUCTION

Craniofacial pain is a medical issue related to several diagnostic and pain treatment specialist fields which include neurologists, physiatrists as well as doctors of dental medicine*(1, 2)*. The most common types of non-odontogenic orofacial pain are temporomandibular pain and musculoskeletal pain related to masticatory muscles and temporomandibular joints *(3, 4)*.

TMJ disorder is an umbrella term for several TMJ diagnoses, the most common being osteoarthritis (OA) and disc displacement (DD) *(5–8)*. Apart from the musculoskeletal pain of the orofacial region, headaches are the most common neurological pain *(9–11)*. Also, musculoskeletal diseases can develop in other anatomically-topographically approximate areas, particularly in the form of cervicogenic and cervicocephallic syndromes *(12–14)*.

Clinical diagnostics of TMJ disorders are related to the existence of another type of headache, particularly since a special diagnosis of TMJ-related headache according to research criteria for temporomandibular disorders (RC/TMD) was introduced *(15, 16)*. On the other hand, cervicogenic orofacial disorders (headaches) can be viewed in co-morbidity with TMJ disorders. Other most common primary headaches (migraine, tension headache) were also found in TMJ patients *(17–22)*.

Magnetic resonance imaging (MRI) is the gold standard in TMJ disorder diagnostics *(23–25)*. Reversible treatments are the primary choice for the treatment of TMJ disorders, with the occlusal splint and TMJ physical therapy both equally successful *(26–28)*.

The aim of this study was to compare the relationship between clinical characteristics of the patients from the subgroup with osteoarthritis (G–1) and patients with disc displacement (G-2) of TMJ related types of headaches and with one-year-follow-up after treatment.

MATERIAL AND METHODS

The study included 105 patients (mean age 37.8±12.8, 90% women) diagnosed with a TMJ disorder that came to the Department of Removable Prosthodontics at the School of Dental Medicine in Zagreb where their treatment and recalls were carried out. The patients were divided into two subgroups according to different diagnoses of TMJ disorders; the G1 subgroup consisted of 70 patients with OA of TMJ (mean age 48.8±14.5, 94.3% women). These patients were compared to the G2 subgroup of 35 patients who only had DD of TMJ (mean age 27.6±11.1, 85.7% women).

Clinical part of the study

Clinical examination was performed based on the DC/TMD protocol and by manual functional analysis (MFA) according to Bumann and Groot Landeweer *(15, 29, 30)*. The main clinical symptoms were pain in the TMJ (that is in the preauricular region) with limited mouth opening and noticing of noise (crepitation, clicking). Patients with the following traits were excluded: previous trauma resulting in mandibular and/or maxillary fractures, rheumatoid or psoriatic arthritis, facial or jaw anomalies, severe acute, chronic or malignant illnesses or wearing an orthodontic appliance during the diagnostic period. The entire study was approved by the Ethics Committee of the School of Dental Medicine, University of Zagreb and all of the patients gave a written consent for the participation in the study.

The duration of TMJ pain from the onset until the first examination was recorded (in months). Pain in the TMJ was measured on a visual-analogue scale (VAS, 0 – no pain, 10 – strongest experienced pain). Occurrence of TMJ noise was recorded on active mandibular movements and it was recorded during dynamic and passive mandibular manipulations within the MFA. The G1 subgroup of patients with OA was determined by crepitations, whereas the patients from subgroup G2 who were diagnosed with DD had previous clicking in medical history with limited mouth opening and no current clicking and current clicking in the TMJ.

Diagnoses of headache and cervical syndromes (cervicobrachial syndrome, cervicocranial syndrome, cervical syndrome) were made based on previous medical history, examination and diagnosis by a neurologists and physiatrist-rheumatologist. Special attention was paid to the occurrence of headache related to TMJ disorder symptomatology, according to RC/TMD criteria *(15)*.

Definitive diagnoses

Definitive clinical diagnoses of all the patients' TMJs were made by MRI imaging of joints at the Department of Diagnostic and Interventional Radiology, Clinical Hospital Center 'Sestre milosrdnice'. The criteria for OA were subchondral sclerosations with or without preserved cortical bone contours. DD was determined according to disc position within the articular fossa, that is, by the anterior position with respect to the narrowest distance between the condylar head and posterior contour of the tuberculum.

The superconductive magnet device 'Avanto' with 1.5 T magnetic field by Siemens (Erlangen, Germany) was used. MRI parameters for the oblique sagittal view of TMJ for T1-weight image were the followng: time of echo 9.4–15 ms, time of repetition 380–410 ms, field of view 180x180, and matrix 410x512, and proton density image with: time of echo 90 ms, time of repetition 2800 ms, fiel of view 160x160, and matrix 320x320.

Treatment and follow-up

The patients from both subgroups were treated in the same way using the occlusal splint and physical therapy (*27, 28*). Recall was carried out 6 and 12 months after the first examination at the Department of Removable Prosthodontics, School of Dental Medicine, University of Zagreb.

Statistical analysis

The collected data were encrypted and organized as a Microsoft Office Excel 2010 file on a personal computer. Statistical analysis was performed by using SAS software. Descriptive statistics was used for determining the basic statistical parameters (average values, standard deviations, medians, minimum and maximum values). The following statistical methods were used: t-test, chi-squared test, and Fischer's exact test *(31)*.

Clinical variables (numerical and normative) were compared between the two groups (G1 and G2) as well as within the total number of patients (G1+G2) for particular clinical features in the period of the first examina-

TABLE 1

Distribution of the share of patients according to treatment success after 6 months (recall T1) and after 12 months (recall T2) between the examined patient subgroups.

Subgroup of patients	Recall	No discomfort	Discomfort	Minor pain	Pain without improvement	Total
G-1	T1	18 (25.71%)	15 (21.43%)	26 (37.14%)	11 (15.71%)	70 (66.67%)
	T2	24 (34.29%)	21 (30%)	14 (20%)	11 (15.71%)	
G-2	T1	3 (8.57%)	7 (20%)	14 (40%)	11 (31.43%)	35 (33.3%)
	T2	7 (20%)	13 (37.15%)	9 (25.71%)	6 (17.14%)	

G-1, patients with osteoarthritis; G-2 patients with disc displacement of temporomandibular joint

TABLE 2

Distribution of patients between the examined subgroups according to the types of headache.

Subgroup of patients	No headache	Tension headache	Migraine	Cervicogenic headache	Headache related to TMJ	Total
G-1	38 (54.29%)	7 (10.00%)	11 (15.71%)	11 (15.71%)	3 (4.29%)	70 (66.67%)
G-2	16 (45.71%)	5 (14.29%)	8 (22.86%)	2 (5.71%)	4 (11.43%)	35 (33.3%)

TABLE 3

Distribution of the total number of patients according to the occurrence of headache and diagnosis of cervical disorder.

Variable	No cervical disorders	Cervical disorders	Total
No headache	38 (36.19%)	17 (16.19%)	55 (52.38%)
Headache present	18 (17.14%)	32 (30.48%)	50 (47.62%)
Total	56 (53.33%)	49 (46.67%)	105 (100%)

TABLE 4

Distribution of certain types of headaches depending on cervical spine disorders in the total sample of both patient subgroups.

Variable	No headache	Tension headache	Migraine	Cervicogenic headache	Headache related to TMJ	Total
No cervical disorders	37 (35.24%)	5 (4.76%)	10 (9.52%)	1 (0.95%)	3 (2.86%)	56 (53.33%)
Cervical disorders	17 (16.19%)	7 (6.67%)	9 (8.57%)	12 (11.43%)	4 (3.81%)	49 (46.67%)
Total	54 (51.43%)	12 (11.43%)	19 (18.10%)	13 (12.38%)	7 (6.67%)	105 (100%)

tion (T0) and on two recalls: after 6 months (T1) and after one year (T2).

Previous pain duration (in months), pain on VAS in TMJs, active mouth opening (in mm), bruxist activity (no, yes), occurrence of headache (no, yes; and certain types of headache: tension headache, migraine, cervicogenic headache, TMJ-related headache), existence of cervical syndromes and polyarthritis (no, yes) were recorded

at T0. Pain on VAS was measured at T1 and T2. Subjective treatment success was determined as: condition without discomfort, discomfort in TMJ, less pain than at T0, unchanged pain intensity compared to T0.

The reliability of MRI assessment was evaluated for each diagnosis of DD on the basis of two researchers' (a radiologist's and a dentist's) inspection by means of Kappa statistics (*31, 32*), which was conducted on MRI images independently of the clinical signs of 12 patients, twice on the same MRIs of both TMJs. Using Cohen's kappa statistics, the interexaminer agreement was measured between 0.8 and 1.0 for MRIs.

RESULTS

There was a significant age difference (t-test=7.632 (df103) with p<0.001) between the two subgroups of TMJ diagnoses, however there were no differences in pain during the follow-up period. In the beginning, the pain on VAS at T0 for G-1 amounted to 6.5 and for G-2 it was 6.1 (t-test=1.3977 (df103) with p=0.2175). During the first recall (T1) pain on VAS for G1 was 2.3, and for G2 it was 3.3, which had borderline statistical significance (t-test=–1.9155 (df103) with p=0.0582). During the T2 recall pain intensity was much lower but without significance in the subgroups: pain on VAS for G1 was 1.6, and for G2 was 1.7 (t-test=–0.2984 (df103) with p=0.7660).

The applied treatment modalities at T1/T2 achieved TMJs without pain in 47.14%/64.29% of patients from G-1 and in 28.57%/57.15% of patients from G-2 (Table 1). There were equal shares of patients without headache (G-1 54.3%; G-2 48 %; chi-squared test (df1)=0.3055 with p=0.5805). The share of certain types of headaches in both groups was 55 tension headaches (52.38%), 11 migraines (10.48%), 13 cervicogenic headaches (12.38%), and headache related to TMJ-disorder in 7 patients (6.67%). There was no statistical significance in the distribution between the G-1 and G-2 subgroups of patients (Fisher's Exact p=0.2792; Table 2).

In the subgroup with OA (subgroup G-1), 51.4% of patients suffered from cervical spine disorders whereas only 34.3% of patients from G-2 suffered from the same disorders. There was a statistically significant difference (chi-squared test (df1)=11.5227, with p<0.0007; Table 3) regarding the total sample of patients (G-1+G-2) depending on the occurrence of headache. The distribution of certain types of headaches depending on diagnosed cervical disorder is statistically significant (Fisher's Exact Test p=0.001; Table 4).

DISCUSSION

The term TMJ disorder encompasses a series of different diagnoses involving musculoskeletal diseases manifested in the stomatognathic system.Although clinical diagnostics is of primary importance to musculoskeletal disease diagnostics, the variability of symptomatology, apart from the generally present joint pain, makes the final diagnosis difficult (*2–4, 33*). On the other hand, the use of MRI and other radiological procedures is impossible in everyday practice. Due to that, a system of unified diagnostics has been developed and in the latest revision it was called RC/TMD (*15, 16*).

There are two main diagnoses in the unique population of patients with TMJ disorder, DD and OA (*6–8*). This study also confirmed that patients with OA of TMJ had higher mean age. As opposed to clinical studies, there is a problem with determining the diagnosis in joints with only arthralgia and therefore MRI remains the gold standard in TMJ diagnostics. Manfredini *et al. (7)* determined the mean age for the subgroup with DD which was 32.7 and the mean age for OA patients which was 54.3 years, both values higher than the age values in this study. Also, the predominance of females was confirmed, up to 91.3%.

Along with the main symptoms of TMJ, secondary diagnostic symptoms are also mentioned, otalgia being one of the more significant ones, but also headaches. However, those are not pathognomonic symptoms and the symptoms related to the ear are also viewed as a part of otorhinolaryngological diagnostics (*33*), whereas headaches have a greater significance for neurological diagnostics of orofacial and craniomandibular pain (*9*). Primary headaches are mainly related to myogenic TMDs and not arthrogenic ones (*20*) and this is supported by the results of the recent study: more than half (52.5%) of all patients do not have headaches at all and cervicogenic headache is typical for OA patients.

Headache as a symptom was significantly more frequent in TMD patients than in the group of non-TMD subjects (*20*). Plesh *et al.* (*19*) mention the five times greater prevalence of migraine (20%) in female patients who are twins which is connected to the occurrence of TMDs, also predominant in women and it has a genetic background *(22).*

Two groups of arthrogenic TMD patients were compared in this study and there were no differences between them although more patients with DD of TMJ (G-2 subgroup) had migraine and TMJ-related headache. The results of this study are not completely comparable to previous studies with the same subject because a recent study used a new diagnosis of 'TMJ contributed or related headache' which better explains orofacial pain bordering between TMJ arthralgia and tension headache. The complex nature of the trigeminal system sensory features is obvious in the mandibular and maxillary involvement in migraine pain and this should be taken into account in differential diagnostics (*21*).

The neuroanatomical basis for the interaction between the orofacial (trigeminal sensory area) and the cervical region is evident from the assumption that the sensory nerve fibers in the centrifugal tract of the trigeminal nerve interact with sensoryfibers from the upper cervical roots belonging to the trigeminocervical nucleus. Cervicogenic headache is often related to myofascial disturbances which can also affect masticatory muscles. The prevalence of cervicogenic headache in the sample of patients at pain management clinics was around 20% and four times higher in women (*12*); which was also shown in our study for patients with OA of TMJ (15.7%).

There was no consensus for the confirmation of the interdependence between TMJ disorder and cervical spine disorders (*14*). Hyperlordosis of cervical spine was determined in patients with TMDs but without definitely confirming the risk of its occurrence *(18).*

There is an existing opinion that there was potential interdependence between asymptomatic DD of TMJ, which would correspond with cervical spine disc prolapse (*34*). Parallel follow-up of TMJ treatment by occlusal splint and of the spinal parameters (spinal pain and mobility) revealed simultaneous significance of healing (*17*). Michigan occlusal splint is considered to be the optimal reversible means of occlusal orthosis and it has been shown to significantly reduce pain in the TMJ along with physical therapy. However, similarly to our study, there were no differences in the influence of TMJ treatment on the entire treatment success (*26–28*). Patients of younger age with lesser cervical spine disorders (patients with DD, subgroup G-2) have equal possibilities of treatment success as the subgroup of patients who are older and with greater cervical spine involvement in painful syndromes.

Although TMD diagnostics using the standardized DC/TMD protocol enables us to compare different researches, in order to make a definitive diagnosis, MRI is needed (*23–25*).

In conclusion, among patients with TMJ disorder there are two age groups: patients with OA (G-1) are significantly older. Pain intensity and treatment success do not vary within the observed groups. Cervical disorders and the related headache are dominant in G-1 patients. Migraine and TMJ-related headaches are more common in patients from G-2. Treatment failure in both patient groups was almost equal, between 15.7% and 17.1%. The analysis of the total sample showed that patients with cervical spine disorders had more headaches.

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Attenuation of systemic inflammatory stress response after preoperative analgesia with clonidine compared to levobupivacaine-a randomised clinical trial

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Abstract

Background and Purpose*: Use of analgetics before the pain stimulus (preventive analgesia) obstruct development of neuroplastic changes in central nervous system, and reduces pain. Furthermore, preventive analgesia can block harmful central nervous system response and inflammation as an early consequence of operation as well. Investigation hypothesis is that preoperative central clonidine will reduce systemic inflammatory stress response better than levobupivacaine.*

Materials and Methods:*. Patients were allocated to three groups, according to preoperative epidural use of 5 μg/kg clonidine (n=17), 0.25% levobupivacaine (n=12) or saline as control group (n=13). Before operation, 1 h after the beginning, 1 h, 6 h, 12 h and 24 h after the operation following parameters were analyzed: procalcitonin (PCT), interleukine-6 (IL-6), C-reactive protein (CRP) and lactate.*

Results: *There were no significant differences between groups in age, gender, body mass index and operation time. We demonstrated significant reduction in PCT, IL-6, CRP and lactate levels in preoperative clonidine group, compared to preoperative levobupivacaine group and controle group. Conclusion. These results support importance of clonidine central effect on pain pathways and systemic inflammatory stress response blockade.*

INTRODUCTION

Investigations showed that rising production of prostaglandine E2 and interleukin-6 at central sites is an important component of surgery induced inflammatory response in patients. Postoperative period is associated with an increased production of cytokines, which augment pain sensitivity. Use of analgesics for immunomodulation can improve patient recovery *(1, 5, 9)*.

Preventive analgesia is based on the concept that the occurrence of strong pain stimulus, hyperexcitation and hyperalgesia are possible to prevent by early blockade of pain pathways *(1, 2)*. Prolonged pain stimulus leads to secondary neuroplastic changes in the central nervous system, known as central sensitization, resulting in exaggerated response to afferent pain stimulus and amplification of pain (hyperalgesia). Administration of analgesics before the pain stimulus or surgical trauma, prevents harmful central nervous system response and inflammation as an early consequence of operation as well *(3, 4)*. In order to achieve success, preventive analgesia should meet two important

conditions, i.e. complete suppression of the afferent pain stimulus and adequate duration in the early postoperative course *(4)*.

Clonidine is an a_2-adrenergic agonist with known sedative, analgesic and hemodynamic properties. It inhibits transmission of nociceptive stimuli in the dorsal horn of the spinal cord, acting on the inhibitory descending pathways *(5, 6)*. Nader et al. showed that preoperative peroral administration of clonidine reduced TNF-alpha level in plasma and cerebrospinal fluid *(7)*. Investigation of Wu et al. reported reduced IL-1RA, IL-6, IL-8 and postoperative pain levels during and after operation, associated with preoperative epidural clonidine treatment *(8)*.

Investigations of long-acting local anesthetic levobupivacaine administered by epidural and intrathecal route provide evidence for improved postoperative analgesia with reduced analgesic consumption *(10, 11, 12, 13)*. But, it remains unknown if that analgesia is sufficient enough to blockade inflammatory stress response during perioperative time.

The aim of the present study is to investigate hypothesis that preoperative administration of epidural clonidine will attenuate systemic inflammatory stress response better than epidural levobupivacaine. The study was designed to compare clonidine and levobupivacaine, and than both with the control group.

MATERIALS AND METHODS

The investigation was carried out in the double-blinded manner, with due approval from the institution Ethics Committee and an informed consent from all study subjects.

Inclusion criteria were patients with well-defined colorectal carcinoma, without spread of malignant disease, confirmed by colonoscopy and computerized tomography (CT), body mass index (BMI) under 30, and perioperative risk for anesthesia and operation, classified as ASA (American Society of Anesthesiologists) physical status I or II. Exclusion criteria were diabetes mellitus, renal insufficiency (kreatinin level>120µmol/L), liver insufficiency (bilirubin level>20 µmol/L, aspartat-aminotransferase>35 i.j./L, alanin-aminotransferase>35 i.j./L), autoimmune disease, corticosteroid and immunosupressive use, and operation time exceeding six hours.

According to a computer generated randomisation list, 50 patients were randomly assigned for one of three intervention groups. Eight patients were dropped out; one could not have the epidural catheter placed. Finally, 42 patients concluded the study (clonidine group, n=17; levobupivacaine group, n=12, controle group, n=13). On the day before the operation, patients were informed on the perioperative procedure, especially of introducing an epidural catheter for pain therapy. Epidural catheter was inserted at the Th10-L1 level (BRAUN Perifix 20 G catheter, winged 18 G Tuohy needle). Correct positioning was tested using 2 ml 2% lidocaine. Patient was observed for 5 minutes for the development of sensory blockade changes.

One hour prior to skin incision patients received 5 µg/kg of clonidine [Catapres®, Boehringer Ingelheim, Germany] or 7 mL of 0.25% levobupivacaine [Chirocaine®, Abbott S.p.A., Italy] or saline. Epidural catheter insertion and drug administration were performed by the anesthesiologist, who was not involved in the anesthesia maintenance. The operation was performed under general anesthesia using midazolam (0.15 mg/kg), fentanyl (2 µg/kg) and vecuronium (0.1 mg/kg) to facilitate endotracheal intubation, and sevoflurane, nitrous oxide 50% in oxygen, boluses of fentanyl and muscle relaxant for maintenance. After the surgery and recovery from anesthesia, patients were transferred to intensive care unit for continuous monitoring of vital functions and homeostasis. On their demand, upon the pain complaint all patients received boluses of epidural morphine 0.06 mg/kg diluted in 20 mL of isotonic saline.

Before operation (T0), 1 h after the beginning (T1), 1 h (T2), 6 h (T3), 12 h (T4) and 24 h (T5) after the operation following parameters were analyzed: procalcitonin (PCT), interleukine-6 (IL-6), C-reactive protein (CRP) and lactate.

The PCT level was measured using a semi-quantitative immunochromatographic rapid test (BRAHMS PCT-Q, Diagnostica, Berlin, Germany). All samples were centrifuged and examined using 6 drops of serum with enclosed dropper pipette into the cavity of the kit. After 30 minutes at room temperature the PCT concentration range of the sample was determined. A PCT concentration ≥0.5 ng/ml can be seen as a reddish band; the color intensity is directly proportional to the PCT concentration. The validity of the test was checked in comparison of the control band. The PCT ranges were as follows: slightly elevated PCT = 0.5 ng/ml, moderately elevated >0.5 ng/ml, markedly elevated PCT ≥2 ng/ml and severely elevated PCT ≥10 ng/ml.

Measurement of IL-6 was performed with enzyme-linked immunosorbent assay (ELISA), using commercially available kits (Bender MedSystems GmbH, Vienna, Austria). The study of CRP was determined by immunoturbidimetric method on the Olympus AU2700 analyzer (Tokyo, Japan).

A randomisation schedule was computer generated by a biostatistician (not otherwise involved in the study). Statistical analysis was performed using SPSS 15.01 Statistical Package (SPSS Inc, Chicago, IL, USA). Kolmogorov-Smirnov test was used to determine intragroup distribution. For quantitative variables with normal distribution one-way analysis of variance (ANOVA) and

TABLE 1
Patient's characteristics (X±SD).

	Clonidine group	Levobupivacaine group	Control group	P
Age (yr)	64.69±7.779	66.00±8.496	65.08±9.041	0.905
Gender				
Male / Female	11 / 6	7 / 5	8 / 5	0.941
BMI (kg/m^2)	25.65±3.90	25.42±2.867	25.69±2.634	0.975
BSA (m^2)	1.94±0.233	2.04±0.265	2.00±0.173	0.437
Operation time (min)	173.82±30.492	150.00±34.902	168.77±32.527	0.149

*P<0.05

Pearson correlation were used. When ANOVA yielded P<0.05, Scheffe's multiple comparison test was used. Data were expressed as Mean±SD. Variable without normal distribution (PCT) was analyzed with nonparametric Kruskal-Wallis test and Spearman correlation. Data was expressed as median (25th–75th percentile). Qualitative data were compared using the χ^2 test. Statistical significance was set at P<0.05.

RESULTS

There were no significant differences in age, gender, body mass index (BMI), body surface area (BSA) and duration of operation among the groups of patients (Table 1). In preoperative clonidine group, PCT levels remain unchanged, compared to preoperative levobupivacaine group, where PCT inceased at the end of investigation. Statistical differences were found at investigation times T3, T4 and T5 (Table 2).

IL-6 levels were significantly lower in preoperative clonidine group throughout investigation time, compared to preoperative levobupivacaine group. Statistical differences were comfirmed at investigation times T1, T2, T3, T4 and T5 (Table 3). CRP levels were significantly lower in clonidine group compared to levobupivacaine group at T5 (Table 4). Lactate levels were significantly lower in clonidine group compared to levobupivacaine group in investigation time T0, and compared to controle group in investigation times T1, T2, T3 and T4 (Table 5).

DISCUSSION

Patients undergoing major surgical resection are at high risk for postoperative infectious complications. They may benefit from early and efficient perioperative analgesia in order to attenuate systemic inflammatory stress response *(17, 18)*. Epidural clonidine was superior to in-

TABLE 2.
Procalcitonin (PCT) levels.

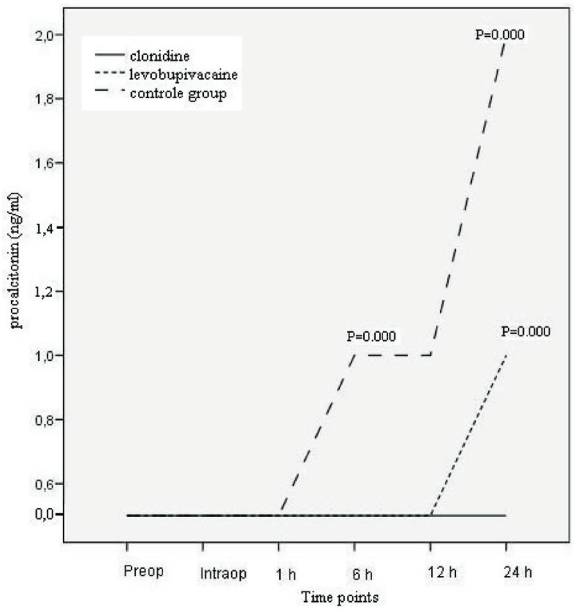


TABLE 3.
Interleukine-6 (IL-6) levels.

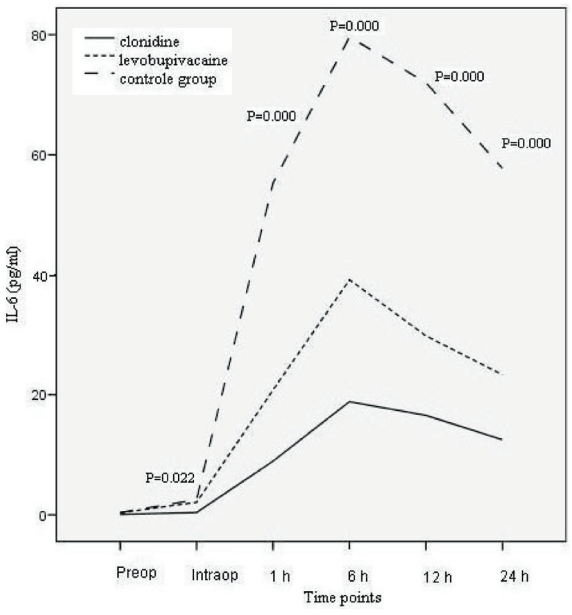


TABLE 4.
C-reactive protein (CRP) levels.

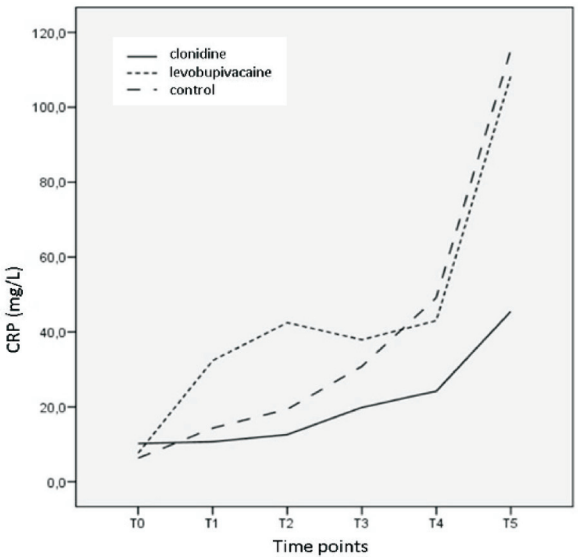
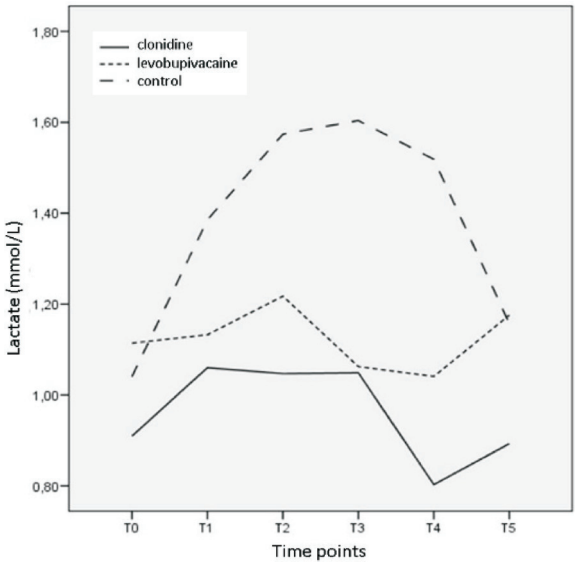


TABLE 5.
Lactate levels.



travenous route in postoperative pain control and immune stress response blockade in investigation of Novak-Jankovic et al., which benefit to his central effect *(5)*.

In our study, clonidine and levobupivacaine were administered by epidural route. We did not observe side effects or complications of epidural analgesia during investigation. Usually, elective surgery induces an increase in PCT after 2 h, rapidly increases between 6–8 h, with highest concentrations at 18 h. The magnitude of elevation is related directly to surgical trauma and inflammation *(3, 4)*. Postoperatively, PCT levels were increased in preoperative levobupivacaine and controle group, but remain unchanged in preoperative clonidine group. These results are similar to those of Sarbinowski et al. who emphasized importance of PCT as an early marker in differentiation of non-SIRS and SIRS patients following major oncological surgery *(18)*, as well as results of Watt *et al. (3)*.

Levels of IL-6 increases proportionally to severity of tissue trauma and inflammation within 1–3 h, with concentration peak at 6 h, and may remain elevated for 48–72 h. In our study levels of IL-6 were significantly higher in levobupivacaine group and controle group, with highest rise at 6 h (T3). The pattern of change of IL-6 was similar to that of PCT, and comparable to results of Mokart *et al. (19)* and Neunhoeffer *et al. (16)*. Levels of CRP and lactate were also lower in preoperative clonidine group, but it was much less prominent.

In conclusion, using the centrally acting a_2-adrenergic agonist clonidine before the pain stimulus has set in resulted in reduced systemic inflammatory stress response compared to levobupivacaine. From the clinical point of view, this effect can contribute to reduction of postoperative complications, which may be a worthwhile advantage to postoperative patients.

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Comparison of minimum effective volume of local anesthetic for ultrasound guided supraclavicular block ($MEAV_{95}$) in elderly and middle aged patients

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Abbreviations:
US – SCB, supraclavicular brachial plexus block
LA – local anesthetic
BP – brachial plexus
MEAV – minimum effective local anesthetics volume
$MEAV_{95}$ – minimum effective local anesthetic volume in 95% of patients
ED_{50} – effective dose in 50% of patients
CSA – cross sectional ar

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Abstract

Background and Purpose: *The aim of this study was to determine the minimum effective volume of local anesthetic (LA) required to produce an efficient supraclavicular block in 95% of patients ($MEAV_{95}$) using an ultrasound (US)-guided technique in an elderly (>65 y) and a middle aged group (<45 y) of patients. Furthermore, we aimed to calculate potency ratio of LA between the groups. We assumed a reduced $MEAV_{95}$ in elderly group.*

Matherials and Methods: *Fourty-four patients (N=22 per group) undergoing upper limb surgery received a US-guided supraclavicular block. The study method is a previously validated step-up/step-down sequential model where the volume of LA for each following patient is determined according to the outcome of the previous block. The starting volume was 30 mL; in the case of block failure, the volume was increased by 5 ml. After successful block, the volume was reduced by 5 mL. $MEAV_{95}$ was calculated using probit transformation and logistic regression. Potency ratio of LA is calculated using Fieller's method.*

Results and Conclusions: *The calculated minimum effective anesthetic volume in 95% of patients was 16.49 mL (95% CI, 12.23–20.75 mL) in elderly and 44.52 mL (95% CI, 19.05–69.99 mL) in middle aged group (95% CI, 0.7–55.3 mL, P=0.044). A potency ratio of LA between middle aged and elderly is 2.69 (95% CI 2.13 to 3.44). The minimum volume requirement for effective US-guided supraclavicular block in 95% of elderly patients was significantly reduced. A potency ratio of 2.69 indicates almost three times stronger LA potency in the elderly.*

INTRODUCTION

Ultrasound-guided supraclavicular brachial plexus block (US-SCB) is widely used for upper extremity surgery because of its ability to anesthetize all four distal upper extremity nerve territories (the median, radial, ulnar and musculocutaneous) at the level of the clavicle. Elderly patients (>65 years) are particularly sensitive to local anesthetics (LA) in peripheral blocks and several mechanisms may account for the increased sensitivity. Conduction velocities, number of large diameter fibers and peripheral nerve (Na+, K+) ATP-ase all decrease with aging and smaller doses of LA are required for regional blocks in elderly patients *(1, 2)*. Up to date, Duggan *et al. (3)* reported the minimum volume required for an effective US-SCB in 95% of patients ($MEAV_{95}$). They performed a study on a population with an average of 48 years of age

and found $MEAV_{95}$ to be 42 ml. Recently we conducted a study where we described structural changes of brachial plexus in the elderly population *(4)*. We observed a significantly smaller surface area in comparison to the younger patients. Also, we determined the minimum volume of LA required for an effective US-SCB in 50% of patients ($MEAV_{50}$) using the Dixon and Massey study protocol. However, in clinical practice, the $MEAV_{50}$ carries little probative value, the $MEAV_{90}$ or $MEAV_{95}$ provide a more accurate measure of the volumes needed to ensure a successful block. The aforementioned structural changes to the brachial plexus in addition to the increased sensitivity that the elderly patients exhibit to LA render the data referring to the minimum anesthetic volume required for an effective US-SCB in 95% of middle aged patients not applicable to the elderly population. Therefore, the aim of this study is to calculate the minimum effective volume of LA (50:50 mixture of 0.5% levobupivacaine and 2% lidocaine) required to produce an effective US-SCB for surgical anesthesia in 95% of patients in elderly patients (>65 years) and in middle aged patients (<45 years) by using logistic regression. We hypothesize reduced LA requirements for the elderly as compared to the middle-aged patients. Since the present study is a dose-response model, the secondary outcome is a potency ratio of LA between the two groups.

MATHERIALS AND METHODS

After we obtained a Hospital Ethics Committee approval for the study as well as a written informed consent from every participant, we recruited 22 elderly (>65 years) and 22 middle aged (<45 years) patients undergoing upper limb surgery to this observer-blinded, up–down sequential allocation study. The study was registered in ClinicalTrials.gov and identifier number NCT01467596 has been issued on the November 4th, 2011. The inclusion criteria were age (>65 years in elderly group and 18–45 years in middle aged group) and a pressumed upper limb surgery in nerve territories of the brachial plexus. Exclusion criteria were the patient's refusal of regional anesthesia, neurologic or neuromuscular diseases, diabetes mellitus and clinical signs of cutaneous infection at the site of needle insertion. We examined all patients with the same ultrasound (Nemio Toshiba Medical System Inc 2001, Japan) with a linear 12 MHz probe. The patients were placed in a supine position with their heads turned opposite to the upper extremity being anesthetized. Brachial plexus is found lateral to the round pulsating hypoechoic subclavian artery that lies on top of the hyperechoic first rib. Prior to performing the block we administered 25 mcg of fentanyl to all patients. We placed a 25G spinal needle (90 mm, Quincke type, Vygon, France) on the outer (lateral) end of the probe and advanced it along the long axis of the probe in the same plane as the ultrasound beam (in plane techniqe). Once the needle tip almost reached the cluster on the ultrasound image, half of the LA volume was injected in proximity to the plexus. We then repositioned the needle cranially in order to distribute the remaining anesthetic volume around the entire brachial plexus cluster. For the purpose of block assessment, we defined time zero as the time of needle removal from the skin. Every 5 min for up to 30 min, a blinded observer checked for pinprick anesthesia with a 23G needle as well as for the loss of cold sensation by applying an alcohol swab in the central sensory region of each nerve location (the median, ulnar, radial and musculocutaneous nerve). The response was compared to the same stimuli delivered to the contralateral arm. We defined a successful block as a total loss of pinprick sensation and total loss of cold sensation in all four regions innervated by the distal nerves assessed within 30 min of LA injection.

The starting volume of the LA mixture was 30 mL. If a successful block was achieved, volume of LA administered to the following patient was reduced for 5 ml. Otherwise, if a complete sensory block in any of distal nerve distributions did not occur, we declared it as failed block and increased the volume administered to the following patient for 5 mL of LA. We first estimated the minimum effective volume required in 50% of patients ($MEAV_{50}$) and then applied logistic regression to calculate the $MEAV_{95}$. We only used the data of unsuccessful blocks to estimate $MEAV_{50}$ and its 95% confidence interval (CI), applying it to the empirical formula of Dixon and Massey for large sample ($x = (\sum f_i x_i / n) + d/2$; x is $MEAV_{50}$; x_i is volume of LA; f_i is frequency of successful or unsuccessful sensory blocks associated with used LA volume; n is the total number of patients with successful or unsuccessful blocks, and d is volume interval-5 ml) *(5)*. We based the sample size calculation on the anticipated mean LA volume from previous studies that analysed US-SCB *(3, 6–8)*. Since our recent study showed structural changes of the brachial plexus in elderly associated with an almost 50% reduction in $MEAV_{50}$ of LA, we presumed a minimum of a 40% reduction of $MEAV_{95}$ in elderly patients. Based on that assumption, we expected a $MEAV_{95}$ of 25

TABLE 1

Demographic Characteristics of Patients.

	Elderly group (N=22)	Middle aged group (N=22)
Age, (years)	74.7 ± 7.1	41.6 ± 5.9
BMI, (kg/m^2) *	26.5 ± 3.5	25.9 ± 2.9
Male/Female, (n)	8/14	13/9
ASA status I/II/III/IV, (n)**	0/5/14/3	7/14/1/0
Surgical time, (min)	76.1 ± 33.9	89.6 ± 33.8

Data are expressed as mean ± SD or n (Number of patients)

* BMI – body mass index

** ASA status – American Society of Anestesiology classification system for assessing the fitness of patients before surgery

ml (i.e. 40% of 42 ml from Duggan' study) with an estimated SD of 10 ml. Such volume difference is also clinically significant (effect size, d=0.6). A probability level of 0.001 and power of 0.90 yielded a sample size of at least 21 patients for each tested group. We performed all calculations using the Minitab 15 statistical software.

RESULTS

Twenty-two patients in each group completed the study protocol. We achieved an appropriate ultrasound visualization of the brachial plexus at the first rib for all patients. The study group baseline characteristics are shown in Table 1. The sequence of successful and unsuccessful US-SCB in elderly group is presented in Figure 1. The same data for the middle-aged group are shown in Figure 2. We calculated effective volumes of 16.49 mL (95% CI, 12.23 – 20.75 mL) and 44.52 mL (95% CI, 19.05 – 69.99 mL) for US-SCB in 95% of patients in the study group and in the middle aged group, resepctively. A potency ratio of local anesthetics between the middle aged and the elderly is 2.69 (95% CI 2.13 to 3.44). The administered volumes ranged from 30 to 5 mLfor the elderly group, while the administered volumes ranged from 35 to 10 mL in the middle-aged group. Nine patients in the elderly group had a failed block. Ten patients in the middle-aged group had a failed block.

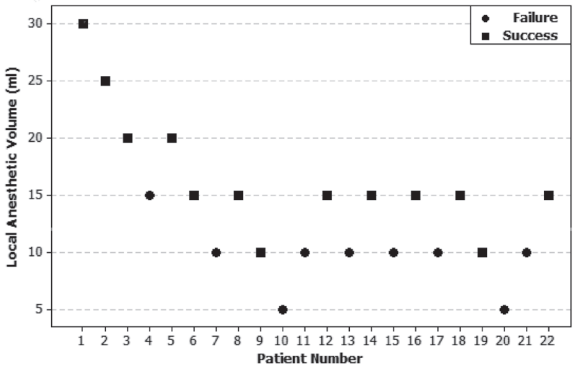

Figure 1. *Up-and-down sequences of US-SCB in elderly group*

Figure 1 presents step-up/step-down sequence model where the local anesthetic volume for the following patient is determined by the outcome of previous block. The starting volume was 30 ml. In the case of block failure, the volume was increased by 5 mL whereas after successful block, the volume was reduced by 5 mL. The calculated effective volume for US-SCB in 95% of patients ($MEAV_{95}$) is 16.49 mL.

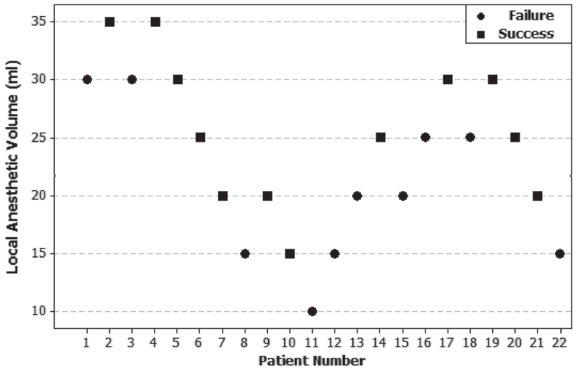

Figure 2. *Up-and-down sequences of US-SCB in middle aged group*

Figure 2 presents step-up/step-down sequence model where the local anesthetic volume for the following patient is determined by the outcome of previous block. The starting volume was 30 ml. In the case of block failure, the volume was increased by 5 mL whereas after successful block, the volume was reduced by 5 mL. The calculated effective volume for US-SCB in 95% of patients ($MEAV_{95}$) is 44.52 mL.

DISCUSSION

In the present study we demonstrated that the calculated minimum effective LA volume required to produce an effective US-SCB in 95% of patients is 16 mL for the elderly and 44 mL for the middle-aged patients thus supporting our hypothesis of a reduced LA volume required for US-SCB in the elderly. We found that the elderly required an approximately two and half times smaller volume of LA mixture for an effective US-SCB in 95% patients in comparison to the $MEAV_{95}$ determined for the middle aged population. On one hand, these results might be explained by the morphological changes of peripheral nerves due to aging, and on the other hand by increased sensitivity of the elderly to LA agents. Aging related structural changes of brachial plexus in supraclavicular region were assessed by measuring the cross sectional surface area as high-resolution sonography appears to be accurate and previously validated tool for the assessment and mapping of the brachial plexus *(6, 9–12)*. The brachial plexus surface area of the elderly patients, as measured at the first rib, is approximately two times smaller than the brachial plexus surface area of the middle aged patients, measured at the same site. We attribute the difference to global involutive changes of the peripheral nervous system that affect brachial plexus as well. Since the area to be blocked was two times smaller in comparison to the middle aged population, we assume that the LA requirements are reduced for elderly patients. Furthermore, the present study explored the dose-response relationship of LA according to different age of patients and we report a potency ratio of 2.69 indicating that LA requirements in middle age are greater by a factor of 2.69. Therefore, a dramatically stronger effect of LA is observed in elderly patients as LA requirements for effective sensory blockade are two and half times lower.

The present study might have some limitations. To date, the majority of published dose-finding studies have focused exclusively on $MEAV_{50}$ and relied on the Dixon and Massey up-down method *(3, 13–16)*. Historically, the up and down methods were employed to investigate the concentration of inhaled anesthetic agents required to

prevent movement upon surgical incision in 50% of patients, the ED_{50} which is also known as minimal alveolar concentration *(17)*. As the concentration-response relation for inhaled anesthetics is steep, the ED_{95} can be estimated using the ED_{50} *(18)*. Furthermore, the sample sizes required by up and down methods are usually small *(17)*. These two factors have contributed to their great popularity. Unfortunately, the dose –response curve of other anesthetic agents differs (for example, LA) and may not be as steep as for inhaled anesthetics. Therefore, the particular Dixon and Massey up and down methodology has recently been criticized as insufficient for accurate determination of LA doses, particularly the extrapolation of the $MEAV_{95}$ number. Tran *et al.* recently published two studies in which the biased coin design was used to approximate minimum effective LA volume for ultrasound guided peripheral nerve blocks *(19, 20)*. However, the present study reports a $MEAV_{95}$ of 16 mL in the elderly and 44 mL in the middle aged patients that strongly correlates with our clinical practice and provides an accurate measure of the volume needed to ensure successful blocks. Therefore, as far as we are concerned, the Dixon and Massey method is still methodologically acceptable, even though it is now becoming a little outdated.

In conclusion, the present study demonstrates reduced requirements ($MEAV_{95}$) as well as a stronger effect of LA in elderly patients.

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Arterial pressure and heart rate changes in patients during "beach chair position" for shoulder surgery: comparison of the regional and general anesthesia techniques

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Abbreviations:
BCP – beach chair position
GA – general anesthesia
ISB – interscalene block
BP – blood pressure
Bpm – beats per minute

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Abstract

***Background and Purpose**: Patients scheduled to shoulder surgery are placed in a sitting position called "the beach chair position" during the operation. This type of surgery can be performed with two anesthetic techniques: general anesthesia or regional anesthesia (interscalene block). This patient positioning is characterized by changes in heart rate and systemic blood pressure. The aim of this study is to show whether the type of anesthetic technique influence the changes in systemic pressure and heart rate in this particular patient position.*

***Materials and Methods**: Retrospective clinical study with reviewed anesthetic charts and medical documentation of the patients scheduled for elective shoulder surgery. Point measurements of systolic and diastolic blood pressure and heart rate were: before surgery, after the positioning of the anesthetized patient, at the end of the operation (lodging of the patient) and then the lowest recorded pressure and heart rate during surgery.*

***Results:** The study included 66 patients in the sitting position for shoulder surgery. Positioning the patients in the beach chair position for shoulder surgery in a population of patients undergoing general anesthesia in relation to the population of patients treated under regional anesthesia, had a significant effect on the decline in systolic blood pressure ($p<0.001$) and dyastolic blood pressure ($p=0.008$).*

***Conclusion**: Regional anesthesia has proven again to be the superior technique over general anesthesia, including cardiovascular stability in patients subjected to shoulder surgery in the beach chair position.*

INTRODUCTION

Shoulder surgery is a common ortopaedics procedure, more often performed in the sitting position called "the beach chair position" (BCP). This position offers the surgeon a better shoulder joint access and visualisation, especially during shoulder arthroscopy. Nevertheless, this position from the anesthesiologist point of view, carries significant risks for the patient. It is known that positioning the patient which is anesthetised, raises a certain issues related to changes in arterial pressure and pulse regulation *(1)*. General anesthesia (GA) is an attenuating factor for physiological regulating mechanisms due to changes of the body position.

Muscular relaxation as well as analgesia and anesthetic drugs contibute significantly to cardiovascular instability *(2)* related to the modification of the autonomic nervous system activity *(3)*. Positioning the awake patient with interscalene block (ISB) performed, also changes the arterial pressure, because of the postural hypotension and the time needed for autonomic nervous system to adjust. It has been noted that some patients with ISB in BCP also have hypotensive episodes during the surgery, which are sudden and often accompanied with profound bradicardy *(4)*.

This type of surgery can be performed with two anesthetic techniques: general anesthesia with mechanical ventilation or regional anesthesia (interscalene block) with or without sedation. Sometimes, these two techniques can be combined. In this study, we compared two groups of the patients, general and regional anesthetic technique and their influence on the changes of heart rate and arterial pressure due to body positioning required for this type of surgery.

MATERIALS AND METHODS

A retrospective analysis of the medical documentation and anesthetic charts was performed for 66 patients undergoing elective shoulder surgery in the beach chair position. Shoulder arthroscopy was done in 46 patients, and open shoulder surgery in 20 patients. General anesthesia with mechanical ventilation was performed in 21 patients, and interscalene block with or without sedation in 45 patients. Every patient was sedated preoperatively with midazolam, with venous access and standard monitoring established (pulse oximetry, electrocardiography and noninvasive arterial blood pressure monitoring).

Induction to general anesthesia was done with thiopental or propofol and neuromuscular relaxation with vecuronium or rocuronium, with dose adjusted to body weight. After the tracheal intubation, the maintenance of anesthesia was done with sevoflurane (Sevorane , Abbot) or isoflurane (Forane, Abbot) in O_2:N_2O=35–40%:65–60%. Intraoperative analgesia was achieved either with fentanyl or sufentanyl.

Interscalene block was performed under the ultrasound guidance (ALOKA ProSound 3, Hitachi Medical Corporation and Hitachi Aloka Medical Ltd., Tokyo, Japan) with 0,5 % levobupivacaine or 0,75 % ropivacaine, with or without 2% lidocaine added, varying the local anestehetic dosage from minimum of 17 ml to maximum of 30 ml. After the skin preparation with chlorhexidine, the ultrasound guided interscalene block was performed. With ultrasound guidance cervical and brachial plexus nerves were visualised between the scalene muscles and the needle was directed towards with the injection of local anesthetic. After the procedure, sensory and motor blockade were evaluated in 10-minutes intervals (warm, cold, touch, pain, movement). During the operation some patients required additional sedation with midazolam, propofol, fentanyl or sufentanyl, but all of them were breathing spontaneusly during the operation.

Four points for measurement of systolic and dyastolic blood pressure and heart rate were analysed: before surgery, after the positioning of the anesthetized patient to the BCP, at the end of the operation (positioning the patient supine) and then the lowest recorded pressure and heart rate during the surgery. Results are reported as mean ±SD and considered statistically significant at the $p<0.05$. Demographic data were descriptively analysed, whereas BP and heart rate values at dedicated time in study for both groups were compared using Two-way ANOVA repeated measures (RM) and Student's t-test for independent samples for comparison of the lowest recorded values of heart rate and BP. Data were analysed using the statistical program Prism 5.03, GraphPad Software Inc., La Jolla, USA).

RESULTS

The study included 66 patients in the BCP for shoulder surgery. Of these, 34 patients were men and 32 women. ASA I – 15 patients, ASA II – 42 patients, ASA III – 9 patients. In 46 patients shoulder arthroscopy was performed and open shoulder surgery in 20 patients. GA with mechanical ventilation was performed in 21 patient and ISB with or without sedation was done in 45 patients. There are no differences in age, weight, intraoperative fluid intake and duration of the operation between these two groups. The two groups of patients were comparable

TABLE 1

Data from 66 patients in the beach chair position. Values are mean ±SD for age, body weight, fluid intake and the duration of the operation and descriptive for sex, hypertension, smoking, and the need for atropine or ephedrine; * p=0.003, Fischer exact test.

	IBS group (n=45)	GA group (n=21)
Age (years)	53,56 ±9,45	51,48 ±11,29
Sex ratio (F:M)	21:24	9:12
Body weight (kg)	81,40 ±14,86	75,62±16,26
Intraoperative fluid intake (ml)	888,89±317,82	1047,62±218,22
hypertension	20	6
smoking	16	5
need for atropine	8	5
need for ephedrine*	2	7
duration of the operation	46,00 ±16,88	44,52 ±15,16

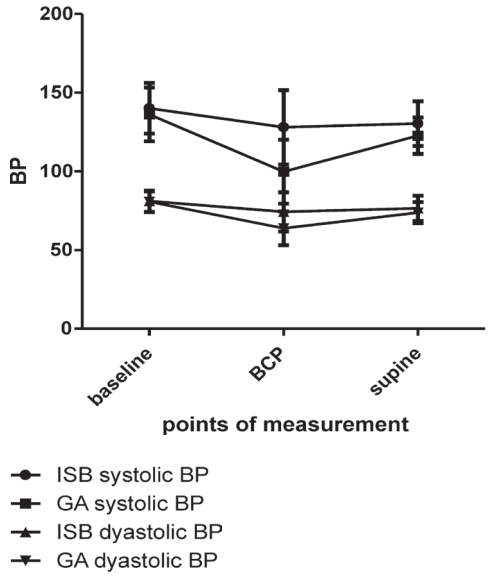

Figure 1. *Comparison of the systolic and dyastolic blood pressure at different points of measurement (baseline, after the positioning of the anesthetized patient in the BCP and at the end of the operation) between the group of patients undergoing GA to the population of patients treated under ISB during shoulder surgery, *p<0.001 (Two-way ANOVA RM)*

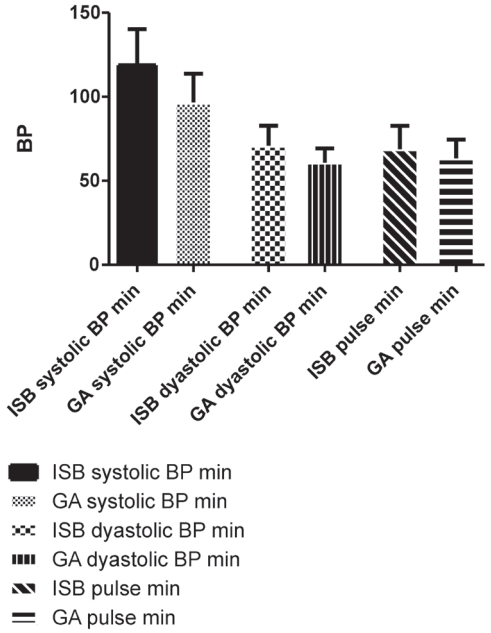

Figure 2. *Comparison between the GA and ISB group regarding the lowest recorded pressure and heart rate during the BCP (*p<0.001; **p=0.001, Student's t-test for independent samples).*

within baseline characteristics. There is a statistically significant difference in the need for ephedrine between groups; the GA group received more ephedrine (Table 1).

When these two groups (GA and ISB) were compared, positioning the patients in the BCP had a significant effect on the decline in systolic blood pressure in a population of patients undergoing GA (99.76 ± 20:28 mmHg) during shoulder surgery in relation to the population of patients treated under ISB (128.00 ± 23.61 mmHg; F (1,64)=14.01, p<0.001, Two-way ANOVA RM; Figure1.). As with systolic pressure, when we compared these two groups, positioning the patient in the BCP had a significant consequence to the dyastolic pressure decrease in the group with GA in comparison to the group with ISB (F (1,64)=7.41, p=0.008, Two-way RM ANOVA; Figure 1.).

Comparing the heart rate values recorded at these four points of measurement, there were no significant difference between groups at any time. (F(1,64)=7.41, P=0.2313, Two-way ANOVA RM). Hypertensive patients were compared with non-hypertensive patients in GA and in ISB group, within the group, and there were no significant difference in BP (both systolic and dyastolic) in any point of measurement, as well as in hypertensive patients compared between the groups.

Comparison betwen the GA and ISB group was done regarding the lowest recorded pressure and heart rate during the BCP . There is a statistically significant difference between the GA and ISB group with both, systolic (t (64) = 4.125, p=0.000) and dyastolic pressure t(64) = 3.429, p=0.001 (Student's t-test for independent samples). There is no statistically significant difference in heart rate between these two groups (t(64) = 1.566, p=0.122, Student's t-test for independent samples) as shown in Figure 2.

DISCUSSION

This study demonstrates significant changes in the blood pressure variations observed during the elective shoulder surgery in BCP, between the two groups of patients (regional or general anesthesia). Patients in this particular position during the surgery are prone to hypotension due to venous pooling and postural hypotension. General anesthesia has a tendency to blood pressure and heart rate variations due to the blunting of the sympathetic nervous system. But, it is not always so easy to find the balance between avoiding too harmful surgical stimuli and keeping the protective role of the sympathetic nervous system for patients.

It is very well known that peripheral nerve blockade offers more cardiovascular stability that general anesthesia, which is again proved in our study. That is not entirely true. There are numerous reports of vehement, profound bradycardia and hypotension which can progress to cardiac arrest *(4),* particularly in patients during shoulder surgery in BCP performed in ISB. This is called the Bezold-Jarisch reflex, and there are many attempts to explain this event. Some authors however doubt that the-

se dramatic events are related to this reflex *(5).* There are some possible explanations in the recent literature related to this occurence: adverse effects of interscalene brachial plexus block, vasovagal syncope, carotid sinus hypersensitivity or orthostatic syncope. Other proposed mechanisms to explain the bradycardia, hypotension, and peripheral vasodilation are that this triad is mediated by activation of some inhibitory reflexes, which have origin with cardiac sensory receptors which leads to stimulation of the parasympathetic and inhibition of the sympathetic activity. This vasovagal reaction could be related to venous pooling (because of the sitting position and epinephrine-induced beta-adrenergic effect) and increased heart inotropy (also beta-adrenergic effects of epinephrine). Epinephrine may be released endogenously due to the reduced venous return and carotid baroreceptor stimulation, or exogenously from epinephrine sometimes administered by the surgeon due to wound infiltration or via the irrigation solution. An empty hypercontractible ventricle, due to increased sympathetic tone, causes stimulation of intramyocardial mechanoreceptors C fibers, withdrawal of sympathetic outflow induces vasodilation and vagal overbalance which leads to bradycardia and hypotension and may be then followed by syncope *(3).* In this study four patients in IBS group had this sudden bradycardia or hypotension. They were all treated with atropin, two of them required repeated doses and one patient lost consciousness, so he had to be intubated. After the operation they all recovered without any neurological deficits.

Questions are raised about the influence of hypotension on cerebral perfusion in these patients during the BCP *(6)* Many authors suggest the additional monitoring in the perioperative period for cerebral perfusion and oxygenation *(7)* in order to anticipate and prevent possible brain damage *(5).*

There are also some proposed maneuvers how to attenuate these events: slowly increasing the angle of the operating table for the elevation in the BCP, allowing the time for the cardiovascular system adaptation. Several studies have shown that if blood vessels can be compressed from the outside (using tight compression garments or military anti-shock trousers), the abnormal heart rate and BP changes can be reduced or eliminated. Surgeons often ask for help from anesthesiologist to induce hypotension for better visualisation and bleeding control, but the safer option is to raise the arthroscopic pump pressure, rather than risk the inadvertent cerebral hypoxia. There is also an issue on blood pressure measurements: how and where to measure the arterial blood pressure in patients which are positioned in BCP. Some authors suggest that measurements should be performed at the level of the brain, for that purpose, because of the large hydrostatic gradient existing between the brain and the site of BP measurement *(1, 8).* According to them, there is a decrease of approximately 2 mm Hg for every inch (2,54 cm) of height difference between the blood pressure cuff and the brain. So, the conclusion drawn from this is that a blood pressure measurement taken with cuff at brachium does not accurately reflect the actual values at the brain level *(9).*

There are some limitations regarding to this study: the major drawback is its retrospective character following different medications used in different dosages, unequal number of participants between the groups and credibility of the recorded BP and heart rate data in the anesthetic medical chart.

To conclude, the regional anesthesia has proven many times to be superior technique over GA during the whole perioperative period for many reasons, including: cardiovascular stability, analgesia, faster recovery and fewer complications. With ultrasound guidance and direct visualisation of the nerves potential neurological damage is minimal. Even though, during the shoulder surgery in the BCP, both in GA or ISB, one must be careful, due to events described in this paper. Monitoring the regional cerebral oxygen saturation in patients undergoing shoulder surgery in the upright (BCP) position, could be an useful tool during routine anesthesia management in order to prevent possible catastrophic events.

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The influence of dexamethasone administration in spinal anesthesia for femur fracture on postoperative cognitive dysfunction

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Abbreviations (in alphabetical order):
ASA = American Society of Anesthesiologists
CAM = Confusion Assessment Method
CI = Cognitive Impairment
DSA = Dexamethasone in Spinal Anesthesia
HPA = Hypothalamic -Pituitary- Adrenal
MCI = Mild Cognitive Impairment
POCD = Postoperative Cognitive Dysfunction
SA = Spinal Anesthesia
VAS = Visual Analog Scale

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Abstract

Background and Purpose: *Cognitive side-effects often complicate postoperative care especially in elderly and fragile patients.The aim of this research is to establish the influence of intrathecal dexamethasone administration in spinal anesthesia with levobupivacaine on postoperative pain, consciousness and values of cortisol levels for patients with femur fracture.*

Methods: *The study is planned as a prospective, interventional, randomized clinical trial. A total of 60 patients ASA2 and ASA3 status, scheduled for surgical procedures will be sorted into two groups and undergo surgery. One group will have spinal anesthesia with levobupivacaine, SA group, and the other study group will have spinal anesthesia with addition of dexamethasone, DSA group. The primary outcome measure is the occurrence of postoperative disturbance of consciousness and plasma cortisol levels. As a secondary outcome measure, we are following pain intensity, blood glucose levels and recovery. Cortisol and glucose are analysed in five measurements. Peripheral venous blood samples are collected before anesthesia, one hour after surgery, third, fifth and on the tenth day after surgery. Postoperative cognitive dysfunction is defined by using Confusion Assessment Method (CAM) criteria. Visual analog scale (VAS) is used to record pain severity among patients.*

Results: *We collected data for 28 patients so far. Preoperative cortisol levels were 713,25nmol/L,pain intensity(VASscore) 8,3. Postoperative cortisol plasma levels in 17 patients in DSA group were significantly lower 384(184-511) nmol/L in comparison to 11 patients in SA group with postoperative cotisol plasma levels 551(397-753) nmol/L. The duration of analgesia in DSA group was 428(350-510) minutes and in SA group 212(183-254) minutes. According to CAM criteria, postoperative cognitive disturbances were seen in 8 (72%) patients in SA group, and 3 (17%) patients in DSA group.*

Conclusion: *The addition of dexamethasone to the local anesthetic has proven so far that it significantly prolongs the duration of sensory block and, thus, decreases opioid requirements and postoperative cognitive disturbances.*

INTRODUCTION

Surgical stress is the systemic response to surgical injury and is characterized by activation of the sympathetic nervous system, endocrine responses as well as immunological and haematological changes *(1, 2,*

3). Spinal analgesia administered before the pain stimulus or surgical injury, prevents harmful central nervous system response and inflammation as an early consequence of operation as well *(4, 5, 6)*. Neuroinflammation is believed to have a role in the pathogenesis on postoperative delirium /confusion and postoperative cognitive dysfunction *(8)*.

Cognitive side-effects such as emergence agitation (EA), postoperative delirium (POD) and postoperative cognitive dysfunction (POCD) are often complicating the postoperative care especially in elderly and fragile patients *(8)*.

The aim of this research is to establish the influence of intrathecal dexamethasone administration in spinal anesthesia with levobupivacaine on postoperative pain, consciousness and values of cortisol levels for elderly patients with femur fracture.

MATERIAL AND METHODS

The research was carried out in the double-blinded manner, with due approval from the institutional Ethics Committee and an informed consent from all study subjects. The study is planned as a prospective, interventional, randomized clinical trial. Inclusion criteria were patients with well-defined fracture femur for surgical procedure in spinal anaesthesia. Exclusion criteria were diabetes mellitus, autoimmune disease, corticosteroid and immunosupressive use. A total of 60 patients ASA2 and ASA3 status, scheduled for surgical procedures were sorted into two groups and undergo surgery in spinal anesthesia with 12,5mg of levobupivacaine, SA group, and with addition of 8mg of dexamethasone, DSA group. The primary outcome measure was the occurrence of postoperative disturbance of consciousness and plasma cortisol levels. As a secondary outcome measure, we followed pain intensity, blood glucose levels and recovery. Cortisol and glucose were analyzed in five measurements. Peripheral venous blood samples were collected before anesthesia, one hour after surgery, third, fifth and on the tenth day after surgery. Postoperative delirium was defined by using Confusion Assessment Method (CAM) criteria. Visual analogue scale (VAS) is used to record pain severity among patients.

RESULTS

We collected data for 28 patients with femur fracture undergoing surgery so far. In DSA group median age was 83 years (range 73-95), and SA group median age was 78 years (range 54-91), 6 patients were ASA 2, 22 were ASA 3. All patients completed the study; there was no statistical difference in patients' demographics.Preoperative cortisol plasma levels in 17 patients in DSA group and 11 patients in SA group were increased (Table 1).

Postoperative cortisol plasma levels in 17 patients in DSA group were significantly lower 384(range 184-511) nmol/L in comparison to 11 patients in SA group with postoperative cotisol plasma levels 551 (range 397-753) nmol/L. The duration of analgesia in DSA group was 428+72.57minutes and in SA group 212+34.76 minutes. A pain-free period in the DSA group was longer than that in the SA group(P<0.001). Receiving time to VAS >6 and the first analgesic dose prescription in the DSA group was significantly longer than that in the SA group (P<0.001) Table 2.

According to CAM criteria some kind of postoperative cognitive impairment was seen in 8(72%) patients in SA group of which we had 5 patients (45%) with moderate cognitive impairment (hyperalert, overly sensitive to environmental stimuli, startled easily) and 3 patients (27%) with mild cognitive impairment (disorganized thinking). In the DSA group we had 3 patients (17%) who developed

TABLE 1

Comparisons of patient's demographic and clinical data with hip fracture.

	Group DSA				Group SA			
	N	Median	Minimum	Maximum	N	Median	Minimum	Maximum
Age (yr)	17	83	73	95	11	78	54	91
Cortisol before block nmol/L	17	713,25	445,10	1020,64	11	639,50	301,15	887,56
VAS before block	17	8,2	5	10	11	8,3	6	10
Duration of surgery (min)	17	114,54	65,15	170,00	11	108,30	63	175

Data presented as median(min-max) measured variables. Age, Cortisol before block, VAS = visual analog scale, duration of analgesia P<0.05

TABLE 2

Comparisons of postoperative cortisol levels, pain level, analgesia duration and POCD.

	Group DSA				Group SA			
	N	Median	Minimum	Maximum	N	Median	Minimum	Maximum
Cortisol after block nmol/L	17	384,56	184,10	511,35	11	551,40	397,05	753,17
Total of analgesia	17	428	350	510	11	212	183	254
VAS 12h postop	17	0	0	0	11	0,60	0	3
VAS 1 postop day	17	1	1	6	11	3,87	1	6
VAS 2 postop.day	17	0,50	1	2	11	2,50	1	5
CAM POCD (%)	17	3	Mild CI 2 (11%)	Moderate CI 1 (5%)	11	8	Mild CI 3 (27%)	Moderate CI 5 (45%)

Data presented as median(min-max) measured variables. VAS postop = postoperative visual analog scale, TA = total analgesia; CAM=Confusion Assessment Method, POCD= Postoperative Cognitive Dysfunction, CI=Cognitive Impairment , P<0.05

mild or moderate cognitive impairment which was due to patients' preoperative cognitive status.

Hypotension was mild to moderate in both groups and was not different.

There was not postdural puncture headache detected. Other complications such as bradycardia, nausea, and vomiting were not different between the two groups and no neurologic deficit was observed in any patients.

DISCUSSION

Femur fracture is a common, mutilating and very expensive health problem. 10% of all fractures are femur fractures and these patients occupy more than 25% of beds in orthopedic hospitals. The mortality rate is very high, and only less than a half of injured people become mobile again after surgery *(1)*. In Croatia, there are about 6000 fractures per year.

These are mainly elderly patients. Approximately 70% of patients will be of ASA physicalstatus 3–4: 35% have one co-morbidity; 17% have two; and 7% have three or more. The most common comorbidities are cardiovascular disease (35%), respiratory disease (14%), cerebrovascular disease (13%), diabetes (9%), malignancy (8%) and treated renal disease (3%) *(9)*.

Approximately 25% of patients with hip fracture have moderate or severe cognitive impairment, and a further 15–25% have mild cognitive impairment. Approximately 25% of patients with hip fractures have at least moderate cognitive impairment (abbreviated mental test score < 7), 20% are institutionalised, and 50% require walking aids or are immobile *(10)*.

Mortality after hip fracture has remained relatively unchanged for the last two decades. Currently, 8.4% of patients die within 30 days of surgery. However, it has been suggested that up to half of postoperative deaths are potentially preventable. Thirty-day mortality is increased for older, sicker, male patients. Up to 15–30% of patients die within a year of surgery *(11, 12)*. The duration of the recovery of cognition after anesthesia and surgery is multifactorial and among other factors is dependent on the type of anesthesia used, the type of surgery and the patient. POCD is considered to be a subtle deterioration in cognitive function, lasting for weeks, months or longer. It can be considered to be a mild cognitive disorder characterized by impairment of memory, learning difficulties and reduced ability to concentrate. Patients are frequently anxious about the surgery they are about to undergo *(13)*.

Major surgery causes an endocrine response with release of hypothalamic-pituitary-adrenal (HPA) and sympathetic nervous system hormones. Cognitive impairment has been associated with high levels of glucocorticoids, as documented in a variety of experimental and clinical studies. Cortisol has been found to be toxic to cells in the hippocampus, and this structure plays a critical role in the consolidation of short-term into long-term explicit memory as well as descending control of the HPA axis. This gave rise to the hypothesis that repeated episodes of stress cause decreased hippocampal inhibition of the HPA axis and, thus, prolonged hyperactivation. It seems that cortisol secretion pattern is profoundly affected (i.e. flattened) by major surgery and this flattening is significantly related to the occurrence of early postoperative cognitive dysfunction *(14, 15, 16)*.

Our early results confirm corellation between increased plasma cortisol levels after fracture with VAS score and cognitive imapairment. Mild cognitive impair-

ment (MCI) is associated with a higher risk of postoperative delirium. Perioperative cortisol and inflammatory alterations observed in MCI may provide a physiological explanation for this increased risk *(13).* Spinal anaesthesia results in less immunosupression, i.e. maintains the number of Th1 cells, thus stimulating the cell immunity *(6).* Recent findings demonstrate a neuroprotective effect of local anaesthetics, leading to significant reduction in cognitive dysfunction after surgery *(4).* Elderly patients > 60 yr of age and undergoing major surgery subjected to general anaesthesia displayed more frequent cognitive impairment during the immediate postoperative period in comparison to those who received a regional technique *(12).* Daniels AH *et al.* showed that many elderly hip fracture patients had unrecognized CI before surgery, and cognitive impairment (CI) patients had significantly more pain than normal cognitive (NC) patients did. Appropriate identification of preoperative CI and treatment of pain are crucial in optimizing patient outcomes. Patients with PreCI have an increased incidence of POCD and cognitive decline. Preoperative CI is a good predictor of subsequent postoperative cognitive dysfunction (POCD) and cognitive decline after 12 months in this group of patients is low *(11).* Dexamethasone added to the local anesthetic and administered intrathecally relieves pain by reducing inflammation and blocking transmission of nociceptive C-fibers and by suppressing ectopic neural discharge *(17).* It has been shown that the duration of postoperative analgesia was prolonged when dexamethasone is given as an adjunct for peripheral nerve blocks *(18, 19).* Although dexamethasone has been used intrathecally for many years, it has not been evaluated when it was given in conjunction with bupivacaine intrathecally. Our investigation confirmed the effect of conjugation of dexamethasone with levobupivacaine the prolong duration time of spinal anesthesia and analgesia compared with spinal anesthesia with only levobupivacaine.

CONCLUSION

The addition of dexamethasone to the local anesthetic significantly prolongs the duration of sensory block and decreases opioid requirements and postoperative cognitive disturbances. There is a need to improve their knowledge around risk factors, prevention and management of postoperative cognitive dysfunction.

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Effects of age on onset time and duration of sensory blockade in ultrasound guided supraclavicular block

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Abbreviations:
US-SCB, supraclavicular brachial plexus block
LA, local anesthetic
BP, brachial plexus
CSA, cross sectional area

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Abstract

Background and Purpose: *Involutive changes of brachial plexus occur with aging. The aim of this study was to determine if these changes would effect onset time and duration of sensory blockade in all four distal nerves of brachial plexus in middle aged (<50 years) and elderly patients (>65 years).*

Materials and Methods: *Middle aged (N=22) and elderly patients (N=22) undergoing upper limb surgery received an ultrasound guided supraclavicular block with a mixture of local anesthetics (50 : 50, 0.5% levobupivacaine, 2% lidocaine). The prospective, observer-blinded study method is a previously validated step-up/step-down sequential model where the local anesthetic volume for each following patient is determined by the outcome of the previous block. The starting volume was 30 ml. Only the blocks with complete sensory blockade in all four regions of distal nerves were analyzed for the onset time and duration of sensory blockade.*

Results and Conclusions: *The mean (SD) block onset time was 25.8±0.6 min and the mean (SD) block duration was 151.5±8.9 min in the entire middle aged group. In the entire elderly group, the mean (SD) block onset time was 21±0.82 min and the mean (SD) block duration was 195.75±14.99 min. The difference in both, onset time and duration was significant (P=0.0002, 95%CI 3.352–6.248; P=0.0023, 95% CI 65.63–22.95, respectively). In conclusion, local anesthetics have a faster onset time and longer duration of sensory blockade in elderly due to alterations of peripheral nerves and increased sensitivity to local anesthetics.*

INTRODUCTION

Ultrasound-guided supraclavicular brachial plexus block (US-SCB) is widely used for upper extremity surgery as it enables anesthesia of all four distal upper extremity nerve territories (the median, radial, ulnar and musculocutaneous) at the level of the clavicle *(1).* Several mechanisms may account for the increased sensitivity of elderly population (>65 years) to local anesthetic agents in peripheral blocks. Conduction velocities, number of large diameter fibers and activity of peripheral nerve (Na+, K+) ATPase all decrease with age. Hence, smaller doses of local anesthetic (LA) agents are required for regional blocks in elderly patiens *(2).* Global involutive changes in elderly population affect brachial plexus (BP) resulting in lower anesthetic volume required for effective US-SCB *(3).* Involutive changes of BP, assessed by measuring the cross-sectional area (CSA) of BP at the first rib, result in significantly smaller CSA in elderly patient as compared with younger patient (0.60±0.08 cm^2 vs 0.91±0.13 cm^2). The study of Paqueron and col-

leagues analyzed influence of age on peripheral nerve blocks *(4)*. They found a positive relationship between age and the duration of a complete sensory blockade. Approximately a 2.5-time longer duration of complete sensory block in the elderly is observed in comparison with young patients indicating that LA agents administered in peripheral nerve blocks have a dramatically different effect on the elderly population. However, they employed ropivacaine, local anesthetic with different pharmacodynamic profile than local anesthetics used in our study. Additionaly, Paqueron et al. analyzed a different type of peripheral block in their study (mid-humeral block). Increased sensitivity to local anesthetics administered for peripheral nerves blocks in elderly in addition to structural changes of brachial plexus led us to believe that sensory block onset time as well as duration of block for each distal nerve of brachial plexus in elderly would be different in comparison with middle aged patients. We hypothesized a shorter onset time and loger duration of sensory blockade in elderly patients.

MATERIAL AND METHODS

After we obtained an approval from Hospital Ethics Committee as well as a written informed consent from every participant, we recruited 22 elderly patients (>65 years) undergoing upper limb surgery to this observer blind, up–down sequential allocation study. We registered the study with ClinicalTrials.gov and were issued number NCT01467596. Exclusion criteria were the patient's refusal of regional anesthesia, any neurologic or neuromuscular disease, diabetes and clinical signs of cutaneous infection at the site of needle insertion. Patients received no premedication before arrival in the operating room and standard monitoring equipment (EKG, noninvasive blood pressure measurement, pulse oximetry) was used during the performance of supraclavicular brachial plexus block. Prior to US-SCB we infiltrated the skin with LA and administered 25 mcg of fentanyl intravenously. We placed a 25 G spinal needle (90 mm, Quincke type, Vygon, France) on the outer (lateral) end of the probe and advanced it along the long axis of the probe in the same plane as the ultrasound beam (in plane technique). We observed the needle movement in real time. Once the needle tip reached the brachial plexus cluster on the ultrasound image, injected the mixture of LA. After administering half of the determined LA volume in „pocket corner", we repositioned the needle cranially toward the neural cluster in order to apply the other half ofthe LA. For the purposes of block assessment, we defined time zero as the time of removal of the needle from the skin. Sensory block onset time for each distal nerve was recorded in 5 minutes intervals during the first 30 minutes after time zero. An observer blinded to volume of administered LA checked for pinprick anesthesia (to a 23-gauge needle) and loss of cold sensation (by the applying an alcohol swab) every 5 min for up to 30 min in the central sensory region of each nerve locations (the median, ulnar, radial and musculocutaneous nerve) in comparison with the same stimuli delivered to the contralateral arm. Duration of sensory blocks for every distal nerve was tested in 30 minutes intervals after surgical completion only for patients with successful blocks. A successful block is defined as complete sensory blockade (total loss of pinprick sensation and total loss of cold sensation) in all four regions of distal nerves assessed within 30 min of local anesthetic injection. The duration of sensory blockade was calculated from onset time to the time of full recovery in all four distal nerves. The starting volume of LA mixture was 30 ml. After a successful block was achieved, the subsequently recruited patient received a reduced LA volume of 5 ml. Otherwise, if complete sensory blockade in any of the distal nerve distributions did not appear, the block was declared as unsuccesful, and the next recruited patient received a volume of LA increased by 5 ml. No further data were obtained from patients with unsuccesful blocks. Unless otherwise stated, the data are expressed with mean ±SD. The unpaired t-test with Welch correction was used to test for the statistically significant differences in mean between the groups. Calculations were performed by software package StatSoft, Inc. (2011), STATISTICA, version 9.1, (Tulsa, OK, USA).

RESULTS

Twenty-two patients completed the study protocol. Appropriate ultrasound visualization of BP at first rib was achieved in all patients. The study group baseline characteristics are shown in Table 1. For the middle-aged patients, the administered volumes of LA ranged from 35 to 10 ml (mean 20 ml). Ten patients in the middle-aged group had a failed block. One patient had incomplete anesthesia in the radial nerve territory. Two patients had failed block in the median nerve and one in the ulnar and median nerve distribution, respectively. Of the six remaining patients with failed block, five had incomplete

TABLE 1
Baseline patient characteristics.

	Elderly group (*n* = 22)	Middle-aged group (*n* = 22)
Age (years)	74.7±7.1	41.6±5.9
BMI (kg/m^2)	26.5±3.5	25.9±2.9
Male/female (*n*)	8/14	13/9
ASA I/II/III/IV (*n*)	0/5/14/3	7/14/1/0
Operated side L/R (*n*)	13/9	8/14
Duration of surgery (min)	76.1±33.9	89.6±33.8

Data are expressed as mean ± standard deviation or *n* (number of patients).
ASA, American Society of Anesthesiologists; BMI, body mass index; L/R, left/right.

TABLE 2

Sensory block characteristics-onset time.

Onset time (min) (<45 g.)	(>65 g.)	N¶ (<45 g.)	(>65g.)	P	95% CI (Confidence interval)
UL N 26.5±3.5	22.5±3.1	16	18	0.0013	1.69–6.30
MDN 25.0±3.3	20.2±3.0	19	20	0.0001	2.78–6.81
RN 25.7±4.0	20.7±4.7	21	20	0.0007	2.24–7.75
MCN 25.9±3.8	20.6±4.6	21	17	0.0004	2.53–8.06
+Group 25.8±0.6	21.0±1.0	4	4	0.0002	3.35–6.24

Data are expressed as mean ± standard deviation or *n* (number of patients).
+ Group (mean ± standard deviation of onset time for the entire group).
¶ N, number of patients with complete sensory blockade in distal nerve territory.
ULN, ulnar nerve
MDN, medial nerve
RN, radial nerve
MCN, musculocutaneous nerve

TABLE 3

Sensory block characteristics-duration of sensory blockade.

Duration of sensory blockade (<45 g.)	(>65 g.)	N¶ (<45 g.)	(>65g.)	P	95% CI (Confidence interval)
ULN 164.6±15.1	213.5±25.8	12	13	0.0001	66.59–31.21
MDN 147.1±23.1	192.7±27.0	12	13	0.0002	24.72–66.47
RN 144.6±23.8	177.3±27.1	12	13	0.004	11.52–53.88
MCN 149.6±24.4	199.6±26.1	12	13	0.0001	29.05–70.95
+Group 151.5±8.9	195.7±15.0	4	4	0.0023	65.63–22.95

¶ N, Number of patients with complete sensory blockade in all four distal nerve territory.
+ Group (mean ± standard deviation of onset time for the entire group).
ULN, ulnar nerve
MDN, medial nerve
RN, radial nerve
MCN, musculocutaneous nerve

block in the ulnar and one in musculocutaneous nerve territory, respectively. For the elderly patients, the administered volumes ranged from 30 to 5 ml (mean 14 ml). Nine patients had a failed block. Sensory block failed in ulnar nerve distribution in two patients, in musculocutaneous nerve distribution in three patients, in ulnar and radial nerve distribution in one patient, in musculocutaneous and median nerve distribution in one patient, in median and radial nerve distribution in one patient and in ulnar and musculocutaneous nerve distribution in one patient. Characteristics of the sensory blockade between the tested groups are shown in Table 2 and 3. For the entire middle-aged group, the mean (SD) block onset time was 25.8± 0.6 min and the mean (SD) block duration was 151.5±8.9 min. The mean (SD) block onset time was 26.5±3.5, 25.0±3.3, 25.7±4.0, 25.9±3.8 for the ulnar, median, radial and musculocutaneous nerve, respectively. The mean (SD) block duration time was 164.6±15.1, 147.1±23.1, 144.6±23.8, 149.6±24.4 for the ulnar, median, radial and musculocutaneous nerve, respectively. For the entire elderly group, the mean (SD) block onset time was 21±0.82 min and the mean (SD) block duration was 195.75± 14.99 min. The mean (SD) block onset time was 22.5±3,09, 20.25±3.02, 20.75±4.66, 20.58±4.63 for the ulnar, median, radial and musculocutaneous nerve, respectively. The mean (SD) block duration time was 213.46±25.77, 192.69±26.97, 177.31±27.12, 199.61±26.17 for the ulnar, median, radial and musculocutaneous nerve, respectively. The difference between onset time of the entire groups as well as every distal nerve and duration of sensory blockade of entire groups as well as every distal nerve was statistically significant, as shown in Table 2 and 3.

DISCUSSION

The present study demonstrated that a LA agents have a faster onset and longer duration of sensory blockade in elderly patients. Both alterations of peripheral nerves propeties due to ageing as well as increased sensitivity of elderly on LA agents might explaine these results *(2, 5)*. Paqueron et al. analyzed influence of age on peripheral

nerve blocks and they found a positive relationship between age and duration of complete sensory blockade. The similarities between present and the study of Paqueron are outcomes that we analyzed (onset time and duration of sensory blockade). Hovewer, our results do not entirely confirm theirs as we found a faster onset time (22 vs. 27.5 min) and a shorter duration of sensory blocks (196 vs. 390 min) in distal nerves of BP in elderly population. Different LA (ropivacaine vs. mixture of levobupivacaine and lidocaine) as well as type of brachial plexus block (mid-humeral block vs. supraclavicular brachial plexus block) between present and Paqueron study make it difficult to directly compare the results. However, we believe that *marked differences in neural architecture and size of surrounding adipose tissue compartments, which are demonstrated between proximal and distal parts of the brachial plexus, are the main reasons contributing to the discrepancies of characteristics of sensory blockade between present and Paqueron study.* The nonneural tissue (stroma and connective tissue) inside and outside the BP increased from proximal to distal, being significant between interscalene/supraclavicular and midinfraclavicular/subcoracoid regions *(6)*. In proximal regions (interscalene, supraclavicular*),* the BP *is surrounded with less fat and stroma within and out of its epineurium than in distal regions (midinfraclavicular, subcoracoid)* which certanly make differences in pharmacokinetics of LA between these two regions.

In conclusion, we believe this finding is of importance for clinicians since elderly patients are frequent in our daily practice, especially in one-day surgery. We should be alert to their increased sensitivity to elderly on local anesthetic agents and should adjust doses of LA agents in order to avoid prolonged sensory blockade in peripheral nerve blocks that can delay discharge from hospital.

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Does rotation thrombelastometry (ROTEM) improve early prediction of coagulopathy in breast tumor?

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Key words: breast disease, breast cancer, benign breast disease, coagulation factors, thrombelastometry

Abbreviations:
TNM – tumor-node-metastasis classification
NST – no special type
NOS – not other specified
ROTEM – rotation thrombelastometry
TEG – Thromboelastography
CT=R – clotting time
CFT = k – clot formation time
MCF = MA – maximum clot formation
AUC – area under the curve
A – Amplitude of cloth formation after 5-30 minutes
PT – prothrombin time
APTT – activated partial thromboplastin time

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Abstract

***Background and Purpose**: Breast Cancer is the second most common cancer among women after skin carcinoma. Incindence in Croatia in 2012 was 2227 new cases per year with mortality 1033 women per year. One of the most pronaunced caracteristics of cancers in general are changes in coagulation factors. Except usual coagulation factors there is thrombelasometry which is dynamic method for evaluation of coagulation factors. We have been used thrombelastometry to see differences in coagulation factors for carcinomas and benign breast diseases.*

***Materials and Methods**: We included 132 patients with benign and malignant breast diseases in Institute of Thumors, Clinical Hospital Center "Sisters of Mersy", Zagreb, Croatia gathered in prospective study in 2012/2013. We compared differences in coagulation parameters with thrombelastometry and usual coagulation factors in earlier mentioned two groups of patients with Mann-Whitney U test what is graficly described with Box and Whiskers plots and correlatio coefficients are described in table with Spearman correlation coefficients.*

***Results:** A5,A10,A15,A20,A25 and A30, MCF and AUC intem are significatly higher in malignant breast disease patients. Significant trend of elevation of these values is present in both patients groups, but those are sigificantly higher in patient group with malignant tumors. While in patients group with malignant tumors almost every correlation coefficients between A5-A30, MCF and AUC intem and cogulation markers are significant, those correlations among patients with benign diseases are not significant. Those values suggests that A5-A30, MCF and AUC intem are significatly correlated with most common used coagulation markers only in patients with malignant diseases.*

***Conclusions:** There are differences in coagulation factors in patients with benign and malignant breast diseases. Trend of elevation of markers of coagulation values is present in both disease, but significantly higher values are in malignant tumor. Our results are based on small numbers and larger number of patients with precise data of coagulation parameters are still needed.*

INTRODUCTION

Breast cancer is the second most common cancer afer skin cancers and it is first cause of death from malignant tumors in women. The most common type of breast is ductal carcinoma (NST) which begins in the linining of the milk ducts. Another type of breast cancer is lobular carcinoma(NOS) which begins in the lobules of the breast. Invasive

breast cancer is breast cancer that has spread from where it began in the breast ducts or lobules to surrounding normal tissue. The incidence in Croatia is around 2300 new cases of breast carcinoma in women with around 800 deaths from these disease in 2013. in University Hospital for Tumors 600 patients had breast biopsy for suspitious breast tumors and afterward therapy after protocol for breast cancer. Surgical treatment have been based on biopsy for suspicious breast tumors and emergency patohistological analysis. Patients with carcinomas are at risk of coagulopathy which can be the first sign of malignant disease.

The hemostatic system with its procoagulant effects mediated directly by cancer cells are considered to play principal role in the development of cancer-induced hypercoagulability and major thromboembolic complications *(1).*

Recently, rotation thrombelastometry (ROTEM) is a method to evaluate the whole process of blood coagulation as a graph from the beginning of clot formation to fibrinolysis providing information related to the cumulative effects of various parameters of all stages of the coagulation and fibrinolytic processes *(2).*

The benefits of ROTEM_ technology include rapid availability of test results and enhanced reproducibility the data which are also continuous, digital, and retrievable for further calculations *(3, 4).*

The goal of the study is to prove connection between changes in coagulation factors and pathystological analysis. In the study standard methods for coagulation factors analysis and thrombelastometry (ROTEM) have been used. Thrombelastometry gives quantitive and graphic measurment from inicial thromb formation to its retraction and lysis. Coagulation factors in correlation with patohistological analysis will contribute to better understanding perioperative treatment of benign changes and malignat breast tumors and more rational thromboprofilaxis and treatment with anticoagulant and antiagregation therapy.

MATERIALS AND METHODS

Using information after prospective study2012/2013. in University Hospital for Tumors, University Hospital Center "Sisters of Mersy", Zagreb, Croatia. Our study have been included 132 patients:59 of those had a breast cancer and all the rest(73) benign breast disease. All patients had mean age 59,15 +- 11,6. This study have been done with aproval of Etical Commity of School of Medicine, University of Zagreb and University Hospital Center "Sisters of Mersy" in Zagreb.All hospitals, pathology laboatories and coagulation parameters laboratories where from University Hospital Center "Sisters of Mersy". Patohistological samples where surgicaly removed by traind specialists for oncologic breast surgery. Patohistological analysis were analysed by trained patologists who are specialised for breast surgery tumors. Mean tumor size were 20,0 +- 11,2 mm. Breast cancer staging was based on pathologic tumor-node-metastasis (TNM) classification. We also analysed therapy after surgery (Chemotherapy, radiotherapy or unknown).

From coagulation factors we analysed FVIII, PC, PT, INR PT. We also used rotation thromelastometry (ROTEM) in all patients and analysed A5, A10, A15, A20, A25, A30 intem, MCF intem and AUC intem. We analysed with differences in this coagulation factors among patients benign and malignant breast diseases.

Patients with preexisting hematological or coagulation disorders, those taking anticoagulants and those with liver or renal dysfunction were excluded from the study.

Sample collection for subsequent coagulation analysis blood samples were drawn into 4.5 ml vacutainers (Becton Dickinson) containing 3.2% trisodium citrate with a citrate/ blood ratio of 1:9. and for platelet count into Becton Dickinson EDTA tubes.

Coagulation analyses

The laboratory tests of coagulation were performed on full automated STA compact device of Diagnostica STAGO for all patients: platelet count, prothrombin time (PT) and activated partial thromboplastin time (APTT), fibrinogen, and D-Dimer. The normal ranges for these tests are: APTT (26–36 s), PT (9.4–15.4 s), Fibrinogen (200– 400 mg/dl), and D-Dimer (0.00–0.50 lg/ml).

ROTEM_ thrombelastographic analysis

Thrombelastography analysis was performed with the ROTEM_ Coagulation Analyzer (Pentapharm, Munich, Germany). Four channels were available for simultaneous measurements. Each test required 300 ll citrated whole blood. The blood was re-calcified with 20 nl 0.2 mol/l CaCl2 (star-TEM_; Pentapharm, Munich, Germany) and activation of coagulation was performed with different agents:

INTEM: Contact pathway activation of the coagulation with 20 nl of contact activator (partial thromboplastin–phospholipid from rabbit brain extract and ellagic acid, in-TEM_; Pentapharm, Munich, Germany).

EXTEM: Tissue factor pathway activation of the coagulation with 20 nl of tissue factor (TF, tissue thromboplastin from rabbit brain extract, ex-TEM_; Pentapharm, Munich,Germany).

APTEM: TF plus 20 nl of aprotinin, plasmin-antagonist (ap-TEM_; Pentapharm, Munich, Germany).

FIBTEM: TF plus inhibition of thrombocytes with 20 nl of cytochalasin (fib-TEM_; Pentapharm, Munich, Germany).

The test starts automatically after injection of the blood sample with an automated pipette and calculated graphical results are obtained by the integrated computer of the device. All ROTEM samples were analyzed within 30–90 min of blood collection.

The following ROTEM_ parameters were determined: clotting time (CT = R) represents a measure of the initiation of clot formation, clot formation time (CFT = k) represents the speed of clot formation, and maximum clot formation (MCF = MA) represents maximum clot strength.

TABLE 1

Descriptive statistics of investigated group.

		N	%
NST	NOS	24	30,5%
	NST	17	40,7%
	Without data	18	28,8%
Tumor grade	1	3	5,1%
	2	35	59,3%
	3	19	32,2%
	Without data	2	3,4%
LumTP	A	4	6,8%
	B	39	66,1%
	Without data	16	27,1%
T	1	5	8,5%
	1b	4	6,8%
	1c	4	6,8%
	2	13	22,0%
	3	2	3,4%
	Without data	31	52,5%
N	0	18	30,5%
	1	5	8,5%
	2	4	6,8%
	3	1	1,7%
	Without data	31	52,5%
M	0	15	25,4%
	1	13	22,0%
	Without data	31	52,5%
Therapy	Without data	15	25,4%
	Chemotherapy	11	18,6%
	Radiotherapy	33	55,9%
Age (years): mean ± SD	59,15 ± 11,6		
Tumor size (mm): mean ± SD	20,0 ± 11,2		

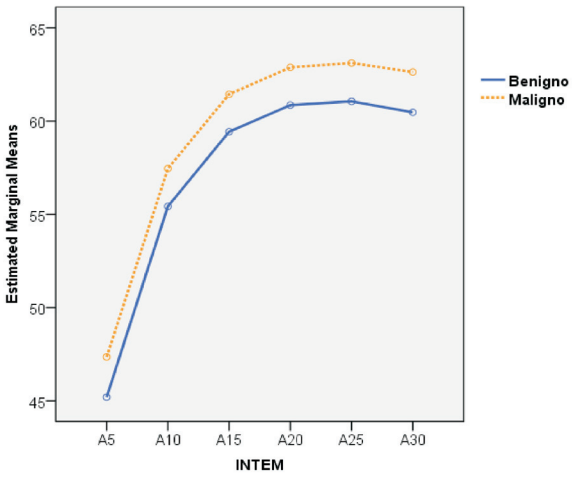

Figure 1. *Differences in A5 – A30 intem values in benign and malign breast disease.*

Statistics

Data were shown in tables in figure. Descriptive stastics were made to describe investigated patients sample Kolmogorov-Smirnov test was used to analyse data normality and due to its results appropriate non-parametric tests were used in following analysis. Differences between patients with malignant and benign breast disease were analysed with Mann-Whitney U test. Correlations between A5-A30, MCF and AUC intem and coagulation markers regarding malignant and benign breast disease were done with Spearman correlations coefficients. All P values below 0,05 were consindered significant. IBM SPSS Stastistics version 19.0.01. had been used as stastistical software (www.spss.com).

RESULTS

Majority of patients: 35 (59,3%) had tumor grade 2, 39 (66,1%) had LumTP grade B. Among those patients that have valid data from TNM clasification (N=28) 13 (46,4%) had T grade 2, 18 (64,3%) N grade 0 and 13 (46,4%) M grade 1 (metastasis in lymphatic nodules). Average tumor size was 20,0 +- 11,2 mm. There was no significan age difference between benign and malignant breast disease group (Z = -0,5; p=0,540; Mann-Whitney U test)

A5, A10,A15,A20, A25, A30, MCF and AUC intem values are significantly higher in malignant breast disease. Table 2. shows descriptive statistics and differences between benign and malignant breast disease regarding A5-A30, MCF, AUC intem and coagulation markers. Significant trend of elevation these values is present in both

TABLE 2

Differences in significant correlations between A5-A30, MCF and AUC intem and coagulation markers regarding malignant and benign breast disease: Spearman correlation.

		Malignant disease				Benign disease			
		N=59				N=70			
		FVIII	PC	PVs	INRPV	FVIII	PC	PVs	INRPV
A5 intem	Rho	0,251	0,149	–0,290	–0,261	–0,005	0,081	–0,040	–0,057
	P	0,055	0,259	0,026	0,046	0,967	0,505	0,741	0,637
A10 intem	Rho	0,256	0,235	–0,334	–0,313	0,072	0,093	–0,075	–0,093
	P	0,050	0,073	0,010	0,016	0,553	0,442	0,537	0,445
A15 intem	Rho	0,298	0,267	–0,332	–0,314	0,100	0,108	–0,090	–0,111
	P	0,022	0,041	0,010	0,016	0,412	0,373	0,458	0,361
A20 intem	Rho	0,289	0,287	–0,334	–0,304	0,146	0,139	–0,135	–0,144
	P	0,026	0,028	0,010	0,019	0,227	0,251	0,266	0,234
A25 intem	Rho	0,316	0,293	–0,330	–0,297	0,200	0,148	–0,145	–0,158
	P	0,015	0,024	0,011	0,022	0,098	0,221	0,232	0,191
A30 intem	Rho	0,314	0,280	–0,310	–0,270	0,222	0,169	–0,168	–0,185
	P	0,016	0,032	0,017	0,039	0,064	0,161	0,165	0,125
MCF intem	Rho	0,284	0,279	–0,326	–0,298	0,180	0,127	–0,128	–0,136
	P	0,029	0,033	0,012	0,022	0,135	0,294	0,289	0,260
AUC intem	Rho	0,311	0,297	–0,326	–0,289	0,219	0,135	–0,117	–0,112
	P	0,016	0,022	0,012	0,027	0,069	0,264	0,336	0,358

group (p;0,001; Friedeman test), but significantly higher values in group with malignant tumor (Figure 1).

While in patients with malignant disease almost every correlation coefficients between A5 –A30, MCF and AUC intem coagulation markers are significant,those correlations among patients with benign disease are not significant. Among patients with malignant disease positive correlations were found between A15-A30,MCF and AUC intem and FVIII and PC. Significant negative correlations were found with PV and INRPV. Different patterns of significant correlations between A5-A30, MCF and AUC intem and coagulation markers regarding malignant and benign breast disease are shown in Table 3.

DISCUSSION

Although breast cancer is one of the most common carcinoma in women there are small number of studies which analyse differences between malignant and benign breast disease with rotation thrombelastometry and correlations between thrombelastometry factors and coagulation factors which we used in our study.

After analyzing all gethered data from our prospective study we concluded that there are strong connection between A5, A10, A15, A20, A25 i A30, MCF and AUC intem with malignant disease and that it is significantly higher in group with malignant diseases than in group with benign breast diseases. Also our values suggests that A5-A30, MCF and AUC intem are significantly correlated with most common used coagulation markers only in patients with malignant disease.

The strength of our study is that we find differencies in specific coagulation parameters with thrombelastometry and standard coagulation tests in patients with malignant disease and we proved significant difference in some specific parameters what we mentioned earlier.

Many studies demonstrates thromboelastographic evidence of hypercoagulability in patients suffering from cancer with a high rate of venous thromboembolic events *(5).*Thrombotic episodes may also precede the diagnosis of cancer by months or years thus representing a potential marker for occult malignancy *(6).* Abnormal hemostasis has been reported in cancer patients, including the shortening of the activated partial thromboplastin time, elevated levels of coagulation proteins (fibrinogen, factors V, VIII, IX, and XI), thrombocytosis, elevated fibrin/fibrinogen degradation products, and an accelerated rate of fibrinogen turnover *(5).*

Hypercoagulability is difficult to detect by standard coagulation tests in cancer patients, but ROTEM *(7),* is

a sensitive method that is able to identify and measure hypercoagulability, which is not detected by routine laboratory tests *(8, 9, 7).* ROTEM, by using whole blood, measures both quantity of clotting and, most importantly quality of clotting which is not recorded by routine coagulation profile (10.4). Hypercoagulability was diagnosed readily by the presence of an accelerated clot formation, as evidenced by shortening of CFT and an increase of the clot strength, as evidenced by increasing of MCF. ROTEM_ tracings on all assays (INTEM, EXTEM, FIBTEM, APTEM) revealed a statistically significant increasing of MCF in cancer patients. While it is likely that certain cancer types are more prone to thrombosis *(11),* we could not predict which tumors are most commonly associated with thrombosis since ROTEM parameters did not differ among cancer subgroups.

In the literature, postoperative hypercoagulability, detected by TEG, has been reported in patients undergoing hepatic surgery *(12),* general abdominal procedures (13, 14), and neurosurgery *(15).* Other clinical settings associated with hypercoagulability detected by TEG include ischemic heart disease *(16),* end-stage renal failure *(17),* insertion of cutdown intravenous catheters *(18)* exposure to oral contraceptives *(19).*

Thromboelastographic analysis of hypercoagulability has been also performed in patients with malignancies in the earlier literature using first the native whole blood TEG and then the celite-activated TEG *(21, 22).* Our findings are by utilizing a newer and more powerful technique, the modified rotation thromboelastogram analyzer, ROTEM_. Hyperfibrinogenemia and thrombocytosis have been frequently reported in patients with malignant disorders *(23, 24).* We therefore sought to correlate these laboratory parameters with those of ROTEM_ and observed that MCF had a strong positive correlation with plasma fibrinogen concentration and platelet counts. MCF measures the maximum clot strength, which is dependent on platelet function and fibrinogen level. The contribution of platelet component and fibrinogen to the clot strenght has been demonstrated in adult patients without tumors *(25, 26, 27, 28).*

Since ROTEM demonstrates hemostasis as a whole dynamic process, ROTEM data gives more information on interaction between platelets and the coagulation cascade rather than the conventional coagulation screens; PT, APTT, platelet count, and fibrinogen concentrations. Identification by the ROTEM of a hypercoagulable state in patients with breast tumor may help to identify those at risk for cancer-induced thromboembolic events and the test may be more valuable if combined with scoring systems for grading deep vein leg thrombosis *(29).* Further investigations that correlate this hypercoagulability with the clinical picture are needed to determine if TEG data can be applied on therapeutic interventions in this patient population.

On the other hand, the limitation of this study are the small number of patients and we recomend to make a larger study with patients with malignant breast diseases which will confirm our data and which will help in future to diagnose breast tumors before even we found them with other diagnostic means. The thing is that coagulation disorders can be one of the first signs of malignant disease and that this can help us to discover the disease in the earlier stage and to make better prognosis in the end.

CONCLUSION

In patients with malignant breast disease almost every correlation ROTEM coefficients between A5 –A30, MCF and AUC intem coagulation markers are significant,but those correlations among patients with benign disease are not significant. Among patients with malignant disease positive correlations were found between A15-A30, MCF and AUC intem and FVIII and PC and significant negative correlations were found with PV and INR. Significant trend of elevation hypercoagulability values is present in both disease but significantly higher values in malignant breast tumor. Rotation thrombelastometry (ROTEM) may improve early prediction of coagulopathy in (benign and malign) breast tumor?

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Patient satisfaction with regional anesthesia in orthopedic surgery

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Abbreviations:
BMI – body mass index
IONV – intraoperative nausea and vomiting
PONV – postoperative nausea and vomiting

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Abstract

Background and Purpose: *The patient satisfaction with perioperative care and anesthesia is important indicator of the quality of the health care system. The evaluation of the patient's satisfaction is a necessity, and the continuous improvement of a quality is important in anesthesia nowadays. It is important to identify the reasons and the risk factors for patients dissatisfaction with anesthesiologic procedures. We conducted this study to asses determinants of regional anesthesia on patient satisfaction.*

Materials and Methods: *This was a prospective observational study which included 164 patients older than 18 years undergoing some orthopedic procedures in regional anesthesia. We noted basic characteristics of patients, important perioperative events and on the following day patients completed a specific questionnaire.*

Results: *Most patients (152/164) were satisfied or very satisfied with the regional anesthesia. Only 11 patients were unsatisfied, and the most common reasons for dissatisfaction were urinary retention, PONV, the multiple puncture attempts and the pain on the puncture site. About 95% patients would receive regional anesthesia again and recommend this kind of anesthesia to the others. We found statistically significant percent (12%) of increasing satisfaction in previously unsatisfied patients ($p < 0,001$).*

Conclusion: *Although, the satisfaction with regional anesthesia in orthopedic surgery in our institution is generally high, there are some factors which can influence on dissatisfaction rate. It is important to identify, monitor and modify them with aim of increasing the overall satisfaction rate.*

INTRODUCTION

The patient satisfaction with perioperative care and anesthesia is important indicator of quality of health care system *(1)*. Patients' satisfaction affects the outcome of health care and the use of health-care services *(2)*. Many hospitals and different health care organizations frequently use patient satisfaction ratings as an integral part of marketing and bench marketing of services. Continuous improvement in quality is important part in all kinds of anesthesia and evaluation of patient satisfaction is a necessity nowadays. It is important to identify the reasons and the risk factors for patients' dissatisfaction with anesthesiologic procedures. Many factors contribute to patient satisfaction, including possibility of choosing the kind of anesthesia, interpersonal relationships, competence of health professionals and a patient's own expectations and preferences *(3)*. Most patients expect uneventful anes-

thesia, but nevertheless, recovery from anesthesia is sometimes complicated by residual sedation, pain, nausea, vomiting or different major and minor complaints *(3, 4)*. These unwished events significantly affects total patient's satisfaction.

Regional anesthesia is becoming a major trend nowadays in many types of surgeries due to many potential benefits. During procedure patient remains conscious with spontaneous respiration and preserved reflexes and aspiration of gastric content is unlikely. Reduction in surgical stress, better postoperative analgesia, and earlier discharge for outpatients and less expense are also valuable advantages. Regional anesthesia and analgesia undoubtedly can improve clinically oriented outcomes *(5)*.

There are many studies in the field of anesthesia about patient satisfaction, but most of them are restricted on general anesthesia. The effect and factors of regional anesthesia on patient satisfaction did not satisfactory demonstrate, so we conducted this study to asses determinants of regional anesthesia on patient satisfaction. The aim of this study was to evaluate patients' satisfaction with previous (regional) anesthesia and to determine predictors associated with unwillingness to have regional anesthesia again in the case of future surgery.

MATERIALS AND METHODS

This was a prospective observational study approved by the University Hospital Osijek Research Ethics Committee. Written informed consent was obtained from each patient. The study population included 164 patients older than 18 years undergoing some orthopedic procedures in regional anesthesia, namely spinal or epidural anesthesia or peripheral nerve blocks. All regional blocks were used as the primary anesthetic technique. We excluded the patients with neurological disorders, psychological diseases, coagulation defects, unlettered patients and those who didn't understand the questions. Also, exclusion criteria were the conversion to general anesthesia or uncompleted data sheet.

This study was conducted by collecting pre-operative, intra-operative and post-operative data on a constructed data sheet divided in three parts. Prior to block administration, attending anesthesiologist entered patient's personal data (age, sex, weight, height, BMI, previous anesthesia experience) in the first part of data sheet. Information about actual regional anesthesia technique (grade of the performer, patient's position during the operation, type of block, the needle size, number of attempts) and intraoperative adverse reactions (need for additional sedation and analgesia, nausea/vomiting, hypotensia or conversion to general anesthesia) were noted in the second part of data sheet by the same investigator at the end of surgery. On the following day, a nurse not belonging to the surgical area and not aware of the anesthesia technique gave third part of data sheet, i.e. a questionnaire to the patient. A questionnaire contain 13 questions about early experiences with anesthesia, satisfaction or dissatisfaction with actual regional anesthesia, willingness to accept regional anesthesia again and about recommendation this kind of anesthesia to the other persons.

Statistical analyses were performed using SPSS software (version 20.0, SPSS Inc, IL, USA). Data normality distribution was tested by Smirnov-Kolmogorov test. Frequency or arithmetic mean and standard deviation were calculated for all data. The difference of numerical variables was analyzed using Student's t-test. Comparison of categorical variables was made with Chi-square test. $P < 0.05$ was considered statistically significant.

RESULTS

A study population includes 164 patients, and 18 patients were excluded from the study. The Table 1 shows demographic data of the study population. Previous experiences with anesthesia had 76% (121/164) patients, mostly general anesthesia (60%), central neuraxial block (29%) or peripheral nerve block (6%). Seven patients didn't remember an anesthesia technique. In this population, 81% of patients (99/121) were satisfied or very satisfied with former anesthesia procedures and only 8 of 121 patients were totally unsatisfied.

Characteristics of actual regional anesthesia technique are described in Table 2. Most of patients (95%) replied that the technique of regional anesthesia was good or very good explained before application. The main reason for choosing a regional anesthesia was the recommendation of attending anesthesiologist in 70% cases. Remaining reasons were: fear of unconsciousness (11%), expectance of less pain after operation (31%), wish to see and hear during operation (22%), wish to eat and drink earlier after procedure (20%), the other people said that is regional anesthesia better than general (19%) or from media became informed that is regional anesthesia better choice (8%). Most of patients (152/164) were satisfied or very

TABLE 1
Demographic characteristics of the study population.

Variable	
Sex (M/F)	77/87
Age (yrs)	47.2±16.75 (18-82)
Height (cm)	171±9.5(150-197)
Weight (kg)	79.9±14.9(52-130)
BMI (kg/m2)	23.3±3.92 (15.9-36.1)

BMI-body mass index

TABLE 2
Characteristics of the actual regional anesthesia.

Variable	N(%)
Provider	
Specialist	138(84)
Resident	26(16)
Type of block	
Lumbosacral spinal/epidural	121(74)
Interscalene block	18(11)
Supraclavicular block	3(2)
Axillar block	15(9)
Femoral block	1(1)
Popliteal block	4(2)
Femoropoliteal block	2(1)
Number of attempts	
1	129(79)
2	24(15)
≥3	11(6)
Needle size	
22 G	11(6)
25 G	91(56)
27 G	27(38)

satisfied with actual regional anesthesia and just 11 patients were unsatisfied.

The reasons of satisfaction or dissatisfaction with actual regional anesthesia are described in Table 3. Prevailing part of satisfied patients s conspicuous from two reasons, i.e. approximately 95% patients have willingness to have regional anesthesia again and would recommend regional anesthesia to the others. Also, we found statistically significant percent (12%) of increasing satisfaction in previously unsatisfied patients with regional anesthesia (χ^2 = 16,806, p < 0,001). Table 4 shows correlation between some variables and satisfaction with regional block.

Need for additional sedation was found in 37% patients, mostly with midazolam 2-5 mg. Also, little portion of patients (23/164) had a need for additional analgesia during surgery, generally with little doses of fentanyl (25-100 mcg). Adverse reactions during surgery were very rare, IONV (intraoperative nausea and vomiting) in only 2 cases and hypotension in 6 patients. Conversion in general anesthesia was done in 3 patients who are excluded from research.

DISCUSSION

Patient satisfaction is an important indicator of health care outcome and evaluation of the quality in anesthesiology *(6, 7)*. We conducted this study to show characteristics and predictors of satisfaction with regional anesthesia among the patients underwent some orthopedic procedures. The main outcome in our research was willingness to accept regional anesthesia again in the future.

In this study we found the high rate (93%) of satisfaction with regional anesthesia and the rate of absolute dissatisfaction was very low (1%). Most former studies in regional anesthesia also reported high levels of satisfaction. Rhee et al. found on 1191 patients underwent spinal

TABLE 3
Reasons of satisfaction or disatisfaction with the actual regional anesthesia.

	N(%)
Reasons of satisfaction	
Consciousness during surgery	88(58)
No pain and sensations during surgery	135(89)
No pain early after surgery	82(54)
Ability to eat and drink early after anesthesia	56(37)
Ability to phone early after anesthesia	97(64)
Reasons of disatisfaction	
Higher number of punctures	4 (23)
Pain during block performing	2(17)
Uncomfortable position during block perfoming	0(0)
Pain during surgery	0(0)
Consciousness during surgery	1(8)
IONV	1(8)
Headache after anesthesia	2(17)
PONV	6(50)
Pain at the puncture site, parestesias, disorders of sensation and motor activity after anesthesia	2(17)
Pain early after surgery	1(8)
Urinary retention	7(58)
Recommendation for laying after spinal anesthesia	7(58)

IONV – intraoperative nausea and vomiting; PONV – postoperative nausea and vomiting

TABLE 4
Correlation between some factors and satisfaction with regional block.

Variables	χ^2	p
Sex	2.434	0.119
Age	0.297	0.862
BMI	0.601	0.741
Presence of pain at the puncture site	5.115	0.024
Provider's experience	0.561	0.454
Number of puncture attempts	3.133	0.077
Position during surgery	3.390	0.335
Explanation of anesthesia procedure	11.205	0.001
Application of sedatives during surgery	0.131	0.717
Application of analgesics during surgery	0.366	0.545

p≤0.05; BMI – body mass index

anesthesia in different types of surgery also high level (96.3%) of satisfaction and 96.8% patients would accept spinal anesthesia in the future *(8).* Jlala *et al*. demonstrated that 88.4% patients were satisfied with regional anesthesia in orthopedic surgery *(9).* In a study of 246 women, Siddiqi et Jafri found high level of satisfaction (81.4%), and the desire to opt for spinal anesthesia in the future (53.7%) among patients receiving spinal anesthesia for cesarean section *(10).* In Kouki et al's Greek study on subpopulation of 63 surgical patients underwent to regional anesthesia, 98.4% described anesthesia procedure as good or excellent. Also, 85.7% of patients with regional anesthesia would like to receive the same anesthetic regimen again in the future *(11).* As it showed in most of studies, level of satisfaction with regional anesthesia was satisfactory high, but this rate can be overestimated because patients like to please medical staff and to meet social expectations by replying satisfied *(8,10).*

The main reasons of dissatisfaction in our study were the recommendation for laying after spinal anesthesia, urinary retention, PONV and higher number of punctures. Our study supports the results of a few former studies. Rhee et al. also found that PONV and postoperative backache were predictable factors for dissatisfaction with spinal anesthesia. Also, likewise to our study, they showed no statistical correlation between satisfaction and age, sex, experience of anesthesiologist, IONV, hypotension and intraoperative application of sedatives and analgesics *(8).* A study conducted by Sindhvananda et al. revealed that post-dural puncture headache, itching and PONV were predictors of dissatisfaction *(12).* Likewise, the main cause of discomfort from regional anesthesia in the study by Bhattarai et al. was reported to be the immobility of lower limbs *(13).* I our study, just two unsatisfied patients marked the immobility of limb as a reason for dissatisfaction.

Statistical comparison between groups of satisfied and unsatisfied patient in our investigation showed no difference in satisfaction scores according to sex, age, BMI, experience of anesthesiologist, number of attempts, position during surgery, IONV, hypotension and intraoperative application of sedatives and analgesics. We found statistical correlation between presence of pain at the puncture site, quality of the procedure explanation and patient satisfaction. Thereby, patients with no pain were more satisfied regarding to those with pain at the puncture site, mostly backache ($\chi^2 = 5.115$, $p = 0.024$). In the study of Siddiqi and Jafri, the patients with lower satisfaction scores with spinal anesthesia complained of a higher frequency and severity of backache *(10).* Choi et al. demonstrated postoperative backache as a risk factor associated with refusing spinal anesthesia in the future *(14).* Also, Rhee et al. found the postoperative backache was one of predictable factors for dissatisfaction with spinal anesthesia *(8).* However, the study of Schwabe and Hopf showed that the backache after spinal anesthesia was not associated with patient's characteristics or technical factors, and apart from preexisting back pain *(15).* Appropriate selection patients for regional anesthesia, reducing the number of puncture attempts, usage of small needles and skilled anesthesiologist could contribute to better satisfaction.

Furthermore, rate of satisfied patients in our study was higher when the quality of explanation of the regional anesthesia procedure was better ($\chi^2 = 11.205$, $p = 0.001$). Also, we found that the main reason for choosing the regional anesthesia by patients was the good recommendation for this technique by attending anesthesiologist in 70% cases. Caljouw et al. found that better informed patients also ranked staff-patient relationship higher, and that the information provision and staff-patient relationship are the major determinants for patient satisfaction with perioperative care *(16).* Dharmalingam et Zainuddin showed on the 200 spinal anesthesias for caesarean section that all the patients were satisfied with the complete explanations provided by the trained personal regarding applicable anesthesia methods *(17).* In another study, Kouki et al. found that the interaction with the anesthesiologist during the intraoperative and immediate postoperative period was the most important element of patient satisfaction for all patients, regardless of the type of anesthesia performed *(11).* Also, Capuzzo et al. concluded that kindness/regard of caregivers" along with "information given by the anesthetist" and "feeling safe" were good indicators for predicting patient satisfaction *(18).*

Our study may have several limitations. First, we didn't use a standardized protocol for performing regional anesthesia and treatment of intraoperative and postoperative adverse effects which can affect on the satisfaction level. Also, our questionnaire wasn't standardized according to most relevant questionnaires in the field of satisfaction with perioperative medicine and anesthesia. We considered that this questionnaire is very easy to understand for most of patients regardless of the level of their education. Third, patients completed the questionnaire second day after surgery when some complications (e.g. postdural puncture headache, neurological sequellaes) were not displayed yet. All these limitations could affect on satisfaction and especially on refusal rates for regional anesthesia in the future.

CONCLUSION

Assessment of patient satisfaction is associated with multiple factors. Satisfaction with regional anesthesia in orthopedic surgery in our institution was generally high. Our study demonstrates that some variables are significant predictors of good satisfaction with regional anesthesia. The presence of some postoperative conditions (i.e. urinary retention, PONV, lying after spinal anesthesia) significantly contribute to patient's dissatisfaction with

regional anesthesia. Fortunately, some of them can be corrected. Intraoperative application of drugs against PONV in risk population, one-time urinary catheterization, skilled anesthesiologist and use of very small needles could minimize these negative conditions and contribute to better satisfaction. Also, good explanation of the procedure and participation in decision making during preanesthetic visit should be the parts of anesthetic plan. Finally, the staff has to identify, monitor and modify the factors which may improve overall patients' satisfaction with regional anesthesia.

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Ultrasound-guided transversus abdominis plane block in combination with ilioinguinal-iliohypogastric block in a high risk cardiac patient for inguinal hernia repair: a case report

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Abstract

***Background and Purpose**: A high risk cardiac patient, ASA IV, was planned for inguinal hernia repair. Since general anaesthesia presented a high risk, anaesthesia was conducted with a transversus abdominis plane (TAP) in combination with ilioinguinal-iliohypogastric (ILIH) block.*

***Material and Methods**: A 70-year old male patient with severe CAD and previous LAD PTCA, AVR, in situ PPM and severe MR and TR 3+, was planned for elective inguinal hernia repair. The preoperative ECHO showed IVS dyskinesis with apicoseptal hypokinesis, global EF 42% and grade III diastolic dysfunction. The patient also suffered from hypertension, diabetes mellitus and had severe stenosis of both femoral arteries.*

Preoperative preparation included IBP monitoring while the TAP block was carried out under ultrasound guidance using an 8 Hertz linear probe. The ilioinguinal and iliohypogastric nerves were identified with ultrasound and peripheral nerve stimulator. Local anaesthetic [0.5% levobupivacaine (Chirocaine®, Abbott Laboratories)] was applied in two locations: in the upper right fascia of the transversus abdominis muscle (15 ml) and around the right ilioinguinal and iliohypogastric nerves (10 ml), totalling a volume of 25 ml. Skin infiltration was performed with 5 ml 2% lidocaine [Lidocaine®, Belupo] and 5 ml of normal saline.

***Results:** Sensory block onset was at 28 minutes after administration and lasted for approximately 18 hours. There were no haemodynamic disturbances and the perioperative course was uneventful.*

***Conclusion:** During the first 18 postoperative hours, the patient was comfortable and satisfied with the anaesthetic procedure.*

INTRODUCTION

Transversus abdominis plane (TAP) block has been used as a component of multimodal analgesia for postoperative pain relief following various abdominal surgeries such as for e.g. hernia repair (1). To improve intraoperative anaesthesia, a combined ultrasound-guided ipsilateral TAP block with ilioinguinal-iliohypogastric (ILIH) block was performed.

Case report

A 70-year old male, high risk cardiac patient, categorized as American Society of Anesthesiologists' (ASA) IV, was scheduled for an elective inguinal hernia repair procedure. He was 84 kg of weight, had a height of 175 cm and a BMI of 27.4, with severe multivessel coronary artery disease (CAD), confirmed by coronary angiography 3 months earlier when he underwent left anterior descending artery (LAD) stenting. Due to severe stenosis of the aortic valve, he also had a biological aortic valve implant with a remaining severe mitral and tricuspid valve regurgitation and a right ventricular systolic pressure of around 50 mmHg. The preoperative ECHO showed an intraventricular septal dyskinesis with apicoseptal hypokinesis and a left ventricular ejection fraction (LVEF) of 42% with grade III diastolic dysfunction. He also had an in situ permanent pacemaker due to third degree AV block. The patient had multiple comorbidities such as long term uncontrolled hypertension, diabetes mellitus and had severe stenosis of both femoral arteries, with a previous femorodistal bypass from the common femoral artery and the superficial and deep femoral arteries of the left side. He also suffered from chronic kidney disease, nephrotic syndrome, hypothyreosis and normocytic anaemia. Medication included a beta-blocker, amiodarone, a calcium channel antagonist in combination with an angiotensin receptor antagonist, moxonidine, aspirin and a high dose diuretic.

MATERIAL AND METHODS

Preoperative preparation included invasive blood pressure monitoring (IBP), continuous electrocardiography (ECG), and pulse oxymetry (SpO2). As with many other regional anaesthetic techniques, the use of ultrasound guidance should be considered to ensure correct needle position and to improve the accuracy of the TAP block technique while limiting the potential for inadvertent damage to the intraperitoneal structures (Figure 1).

The TAP block was performed between the internal oblique and transversus abdominis muscles, using a 22-gauge, 10 cm neurostimulating needle [Stimuplex DÒ, Braun, Melsungen] with one attempt. It was carried out under ultrasound guidance using a linear probe of 8 Hz and a neurostimulator. After that, the ilioinguinal and iliohypogastric nerves were identified medially from the cristae iliacae anterior superior with ultrasound and a neurostimulator set at 1 mA. Local anaesthetic [0.5% levobupivacaine (Chirocaine®, Abbott Laboratories)] was applied in two locations: in the upper right fascia of the transversus abdominis muscle (15 ml) and around the right ilioinguinal and iliohypogastric nerves (10 ml), totalling a volume of 25 ml. Skin infiltration was performed with 5 ml 2% lidocaine [Lidocaine®, Belupo] and 5 ml of normal saline.

RESULTS

Following the administration of the TAP block in the upper fascia of the transversus abdominis muscle, onset of sensory blockade occurred after 28 min. The sensory blockade of the ILIH block occurred earlier, 18 min after the administration of the anaesthetic around the nerves. The testing of the blocks was done with pick prick technique and a temperature discrimination test from the right side of Th 10 to L 1 dermatome. During the operative procedure, the patient was sedated with midazolam 3 mg intravenously (iv). All measured vital parameters such as IBP, ECG/HR and SpO2 were of correct values. The surgical procedure lasted 45 min and was without any

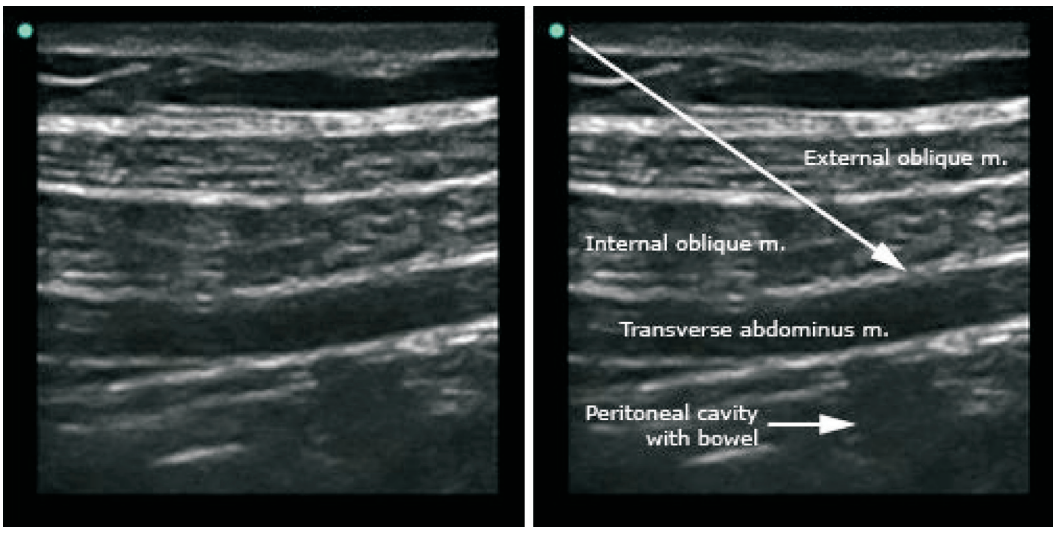

Figure 1. *Sonographic view of the three lateral abdominal muscles. The orientation of the probe was perpendicular to a line joining the anterior superior iliac spine and the inferior rib to obtain a transverse view of the abdominal layers.*

accompanying complications, after which the patient was sent to the post anesthesia care unit (PACU) for continued perioperative monitoring of vital parameters. After one hour in the PACU, all the vital parameters remained within normal values, the arterial cannula was removed and the patient was discharged to the surgical ward. During the first 24 postoperative hours, the patient's pain level was visually monitored using analgesic scales (VAS, 0 = no pain, 10 = worst pain imaginable) every three hours. Sensory block lasted for 18 h postoperatively with a VAS scale value of 2 and after block regression, there was no need for any further analgesia. At the postoperative follow up sessions, the patient reported his experience as without objections and was very satisfied with the anaesthetic treatment. His further course of recovery was also without any complications.

DISCUSSION

Patients with coronary artery disease and multiple coexisting diseases, posted for major abdominal surgery are unquestionably at a high risk for perioperative complications *(2).* We presented a high risk cardiac patient undergoing inguinal hernia repair, with significant comorbidities among which was multivessel CAD, severe mitral valve and tricuspid valve regurgitation, a decreased LVEF and diastolic dysfunction. Local infiltrative anaesthesia or regional blocks are the most suitable techniques in high-risk patients and patients with ASA II–IV status. Since general anaesthesia presented a high risk, a combined ultrasound-guided ipsilateral TAP block along with ILIH block was the technique of choice, with the intention of reducing the possibility of failed block if only one of the blocks was attempted by itself. There is no data thus far to support this combined approach in such a high risk case. Although, TAP was introduced in anaesthesia practice by Rafi *(3)* in 2001., our understanding of the TAP block and its role in contemporary practice remains limited, especially in high risk cardiac patients such as patients with severe mulitvessel CAD. On the other hand, the ILIH block is safer and easier to perform in order to provide analgesia for inguinal surgical procedures, but the drawbacks are that it has a relatively short duration and a relatively high failure rate of 10-25%, even in experienced hands *(4, 5).* Even though the TAP block provided effective analgesia during the first 24 h after surgery, there are no studies to confirm that this block is superior to other techniques of analgesia *(6, 7).* The confirmation of effectiveness of a combination of a TAP block and an ILIH block has been presented previously in other high risk groups such as those with cirrhosis of the liver who were undergoing inguinal hernia repair procedures *(8).* In high-risk patients with CAD, there is always a possibility for deleterious intraoperative tachycardia and significant fluctuations in arterial blood pressure, which may precipitate acute myocardial ischemia if the anaesthesia of choice is not an opioid based technique. In this patient there were no undesired haemodynamic disturbances related to the performed TAP and ILIH blocks.

In conclusion, ultrasound-guided ipsilateral TAP block in combination with an ILIH block in this case, was administered in a high risk cardiac patient, resulting in a successful sensory block, which lasted for 18 h after block administration. After block regression, there was no need for any further analgesic therapy from the side of the patient, neither were there any other complications.

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The application of paravertebral block in high-risk patient with cardiorespiratory, liver and kidney problems: a case report

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Abstract

Background and Purpose: *We present a case report of a patient of the American Society of Anesthesiologists' (ASA) IV scheduled for a modified radical mastectomy (MRM) due to malignant disease. The patient was a high risk patient for general anesthesia and we opted for the application of unilateral paravertebral block on several levels. Case report. A 86-year-old female was scheduled for a surgery due to recurrent malignant process on her right breast. She was an ASA IV patient with chronic obstructive pulmonary disease (COPD GOLD A), respiratory failure, diabetes mellitus, diabetic nephropathy, cirrhosis and chronic laryngitis. Echocardiography showed diastolic dysfunction and pulmonary hypertension of moderate degree. During the preparation for the surgery, an invasive blood pressure measurement was set while the paravertebral space was identified with the neurostimulator using the linear ultrasound probe of 8 Hertz (Hz). The anesthetic [0.5% Levobupivacaine (Chirocaine®, Abbott Laboratories)] was applied in levels of Thoracic (Th) 2, Th3, Th4 and Th5 (5 milliliters(ml.) per level). We used 2% lidocaine [Lidocaine®, FC] for local infiltration at the site of the block.*

Results: *Sensory blockade occurred after 32 minutes (min.) and lasted for about 8 hours (h) with normal perioperative period and hemodynamic parameters without accompanying complications.*

Discussion and Conclusion: *This case report shows that the application of paravertebral block with lower doses of long-acting local anesthetic at several levels leads to a satisfactory anesthetic and analgesic effect while maintaining hemodynamic stability.*

INTRODUCTION

Breast surgeries which involve modified radical mastectomy (MRM) with dissection of the axilla are usually performed under general endotracheal anesthesia with the use of mechanical ventilation. Patients with present significant cardiac and pulmonary problems have a very high risk for the use of general anesthesia. Here we show the American Society of Anesthesiologists' (ASA) IV patient scheduled for modified radical mastectomy (MRM) with malignant disease present. Due to a high risk of general anesthesia, we decided to apply unilateral paravertebralnog blocks on several levels.

Case report: A 86-year-old, 84 kilograms (kg) in weight and 157 centimeters high (cm.) female was scheduled for a surgery due to a recur-

rent malignant process on her right breast. She was an ASA IV patient with chronic obstructive pulmonary disease (COPD GOLD A), respiratory failure, diabetes mellitus, diabetic nephropathy, adipositas, cirrhosis and chronic laryngitis. Auscultationally, she had prolonged expiratory phase with basal groan on both sides. Arterial blood gas analysis and spirometry showed obstructive disorders of moderate degree. The X-ray of the heart and lungs showed pronounced interstitial pattern on both sides with shallow lateral phrenicocostal sinuses. Echocardiography showed diastolic dysfunction with ejection fraction of about 50%, with pulmonary hypertension of medium degree. Electrocardiogram showed left ventricular hypertrophy. The patient has a long history of diabetes with insulin therapy accompanied by diabetic nephropathy and liver cirrhosis.

MATERIALS AND METHODS

Upon the arrival in the perioperative monitoring unit (with prior midazolam medication of 5 milligrams (mg.) intramuscularly (i.m.) in the department) a non-invasive monitoring of heart rate (HR), non-invasive arterial blood pressure (BP), fingertip arterial oxygen saturation (SpO2), and the needle cannula were placed on a patient. Then, the arterial cannula was placed with the infiltration of 1ml. 2% lidocaine [Lidocaine®, FC] using the ultrasound surveillance with in plane technique in the left radial artery for invasive pressure measurements. After the adjustment of the patient in the sitting position and aseptic washing of dorsal surface we detected paravertebral space using linear probe of 8 Hz and a depth of 4.5 cm. The skin and subcutaneous tissue were infiltrated with 1 ml. 2% lidocaine [Lidocaine®, Belupo] per level. In order to perfom a paravertebral block we used an ultrasound and a neurostimulator with neurostimulating needle [Stimuplex D®, BBraun Melsungen] 22 G, 10 cm in length. We used neurostimulators for the detection of paravertebral space of the initial values of 2 Hz and lowered them to 0.5 Hz with the persistence of muscle contraction. After that, we applied local anesthetic 0.5% Levobupivacaine [Chirocaine®, Abbott Laboratories] with the aspiration on the four levels of Th2, Th3, Th4 and TH5 (5 ml. per level) for analgesic and anesthetic effects.

RESULTS

Following the administration of a block, the sensory blockade occurred after 32 min and surgical anesthesia in 40 min. The testing of the block was done with pick prick and warm - cold test from the right side of Th 2 to Th 6 dermatoma. During the operative procedure, the patient was sedated with 3 mg. midazolam intravenously (iv) and 50 micrograms (mcg.) of fentanyl iv. All measured vital parameters: heart rate (HR), fingertip arterial oxygen saturation (SpO2), invasive arterial blood pressure (BP) were of proper values. The surgical procedure lasted 90 min. without accompanying complications after which the patient was sent in the unit for perioperative monitoring with continuous monitoring of hemodynamic parameters and saturation. After 60 min. of normal hemodynamic parameters, arterial cannula was removed and with the instructions to the staff, the patient was sent to the clinic for plastic surgery. During the first 24 postoperative hours, the patient's pain level was visually monitored using analgesic scales (VAS, 0 = no pain, 10 = worst pain imaginable) every three hours. Sensory blockade lasted 8 hours from the application of the block with VAS = 1. After 8 hours VAS = 3 diclofenac 75 mg. iv was applied once, which results after 30 min. in coupling pain and lowering VAS to 1 without a need for re-application of analgesia in any form. At postoperative interviews 48 h after the operation, the patient was very satisfied with the anesthesiologist treatment and no complications occurred.

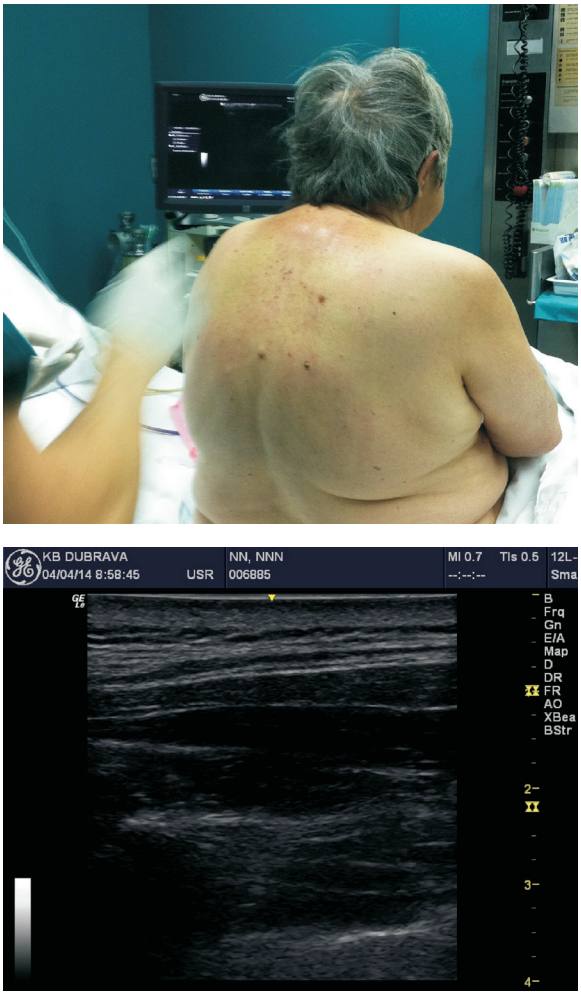

Figure 1. *Patient position and ultrasound image of local anesthetic spread. N = Neurostimulator needle [Stimuplex D®, BBraun Melsungen]; TP = transverse process; EICM = external intercostal membrane; LA = local anesthetic; PL = pleura*

DISCUSSION AND CONCLUSION

This case report shows the application of paravertebral block on ASA IV patient with present significant cardiac, pulmonary, liver and kidney problems. The patient was scheduled for MRM with dissection of the axilla. After the full examination of the patient's condition, we wanted to avoid endotracheal intubation and mechanical ventilation because of possible cardiorespiratory complications. Some of the techniques of regional anesthesia can adequately replace the general endotracheal anesthesia in breast surgeries. One of them is a thoracic epidural anesthesia (TEA) (1.2). This technique can result in bilateral symetrical anesthesia but also in a sympathetic block and frequent hemodynamic instability *(3).* Very important side effects such as nausea, vomiting and hypotension were more common in TEA than thoracic paravertebral block (TPVB) *(4).* There are many papers in favor of anesthesia in breast surgery only in the TPVB or in a combination with general anesthesia *(5-7*). Tahiri et al. show the results of 11 studies that compared paravertebral blocks with general anesthesia. The research has proven significantly lower pain scores during the first 6 postoperative hours and less requirements for pain relief in patients who had paravertebral block applied *(6).* Paravertebral blocks proved to be very useful in reducing the development of chronic postoperative pain *(8).* Although there are many techniques performing paravertebral blocks *(9 - 11),* we have, in order to achieve a better precision in sensory blockade, decided to give blocks on several levels using the ultrasound and neurostimulators in plane technique. Therefore, it should be noted that in a single shot block administration the occurence of very significant problems described as a failed block or epidural spread of local anesthetic *(12)* is possible. With the frequent use of ultrasound, the application of paraveretbral blocks in high-risk patients as a method of choice *(13, 14)* is becoming more common. We had to take into consideration cardio-respiratory problem in our patient, together with the cirrhosis of the liver. It is known that amino - amide local anesthetics are metabolized in the liver and the worse the perfusion and function of the liver *(15, 16)* is, the longer their elimination half-life is. In conclusion, by cautious administration of small doses of local anesthetics (5 ml.) at four thoracic paravertebral levels we achieved successful unilateral anaestetic effect without accompanying cardiorespiratory and metabolic complications.

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The use of an ultrasound-guided supraclavicular brachial plexus block in a high risk patient with cardiomyopathy

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Abstract

With the rapid growth of the elderly population, along with increased comorbidities and greater life expectancy, geriatric surgery has become more frequent and requires careful tailoring of anesthesia technique. Preanesthetic evaluation should concentrate on the identification of age-related diseases and an estimation of physiological reserve. Age-related cardiovascular changes are leading factors impacting perioperative outcomes among elderly patients. The management of a patient with dilated cardiomyopathy, who undergoes a non-cardiac surgery is always a challenge for an anesthesiologist, as this situation is associated with a high mortality rate.

We report a use of the ultrasound guided supraclavicular brachial plexus block in 87-year old woman for revision of wound of left wrist and reposition and immobilization of left forearm and elbow. Her previous medical records revealed that she arterial hypertension, chronic atrial fibrillation with dilated cardiomyopathy and chronic kidney disease, stage II. Postoperatively, she developed respiratory insufficiency.

This case report exemplifies how despite all the measures and precaution we had taken, with choosing anesthesia having only minimal hemodynamic fluctuations and carefully planned and balanced hydration of patient we still had unwanted outcome.

INTRODUCTION

In the last 50 years, the number of people over 65 years of age has tripled in the world. In Europe, they are expected to represent 30% of the population within 40 years *(1)*. With the rapid growth of the elderly population, along with increased comorbidities and greater life expectancy, geriatric surgery has become more frequent and requires careful tailoring of anesthesia technique *(2)*. Aging is a universal and progressive physiologic process characterized by declining in end-organ reserve, decreased functional capacity, increasing imbalance of homeostatic mechanisms, and an increasing incidence of pathologic processes *(3)*. Aging is now viewed as an extremely complex multifactorial process with interaction of various pathways to differing degrees and effect *(4)*. Age is not a contraindication to anesthesia and surgery; however, perioperative morbidity and mortality are greater in elderly than younger surgical patients. Anesthetic risk correlates much better with the presence of coexisting disease than chronological age. Therefore, preanesthetic evaluation should concentrate on the identification of age-related

diseases and an estimation of physiological reserve. Age-related cardiovascular changes are leading factors impacting perioperative outcomes among elderly patients, despite advances in perioperative care cardiac morbidity and mortality remain high ranging from 2-15% depending from the study *(5).*

Case report

A 87-year-old female patient, with 150 cm of height and 50 kg of weight, was hospitalized under diagnosis of fractured left femur neck, left elbow dislocation and fractured left forearm with open wound on the left wrist after she had fallen at home. Indication for revision of wound of left wrist and reposition and immobilization of left forearm and elbow was set.

Her previous medical records revealed that she arterial hypertension, chronic atrial fibrillation with dilated cardiomyopathy and chronic kidney disease, stage II. She was on treatment with amiodarone, trandolapril, metildigoxine and furosemide.

After admission, the patient's initial laboratory reports were: random blood glucose of 7.9 mmol/L, urea 17.4 mmol/L, creatinine 162 μmol/L, sodium 140 mmol/L, potassium 3.8 mmol/L, hemoglobin 132 g/l, hematocrit 42.2%, CRP 80.5 mg/L, and blood coagulation were normal. Her chest X-ray revealed enlarged cardiac borders and clear lung fields [Figure 1].

On preanaesthetic examination her heart rate was irregular, presented as atrial fibrillation with an average ventricular response of 80 beats per minute. Systolic and diastolic blood pressures were 150 mmHg and 90 mmHg, respectively. Her respiratory rate was accelerated with jugular retraction and usage of accessory respiration muscles. She was given ASA IVE status on preoperative examination.

After reviewing medical records and patient examination, a supraclavicular brachial plexus block was chosen because it produces minimal effects on the heart rate, blood pressure and contractility of the heart. It was considered as appropriate form of anesthesia according to the planned surgical treatment and subsequent pain treatment. Before the beginning of the procedure, venous access and standard monitoring was established (pulse oximetry, electrocardiography and noninvasive arterial blood pressure monitoring). After aseptic preparations and under ultrasound guidance brachial plexus was identified and 20ml of 0.75% ropivacaine were administered slowly in 2ml increments with gentle aspiration between doses. After completion of the procedure, sensory (warm, cold, touch, pain) and motor (absence of foot mobility) blockade were evaluated in 10 minutes intervals. Visual analogue scale (VAS) was used for pain score recording. A paralysis of the left arm and VAS score 0 was recorded after 40 minutes and complete block was achieved.

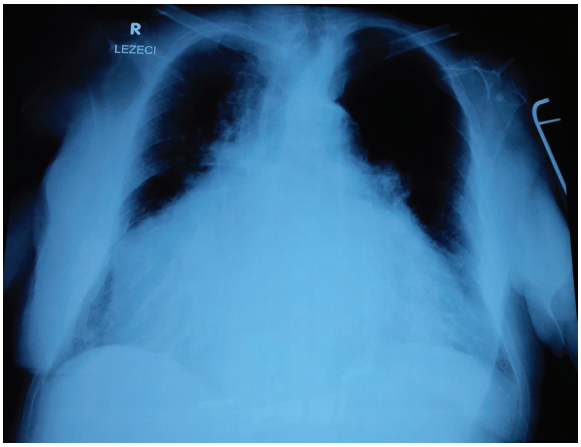

Figure 1. *Chest X-ray at the admission in hospital.*

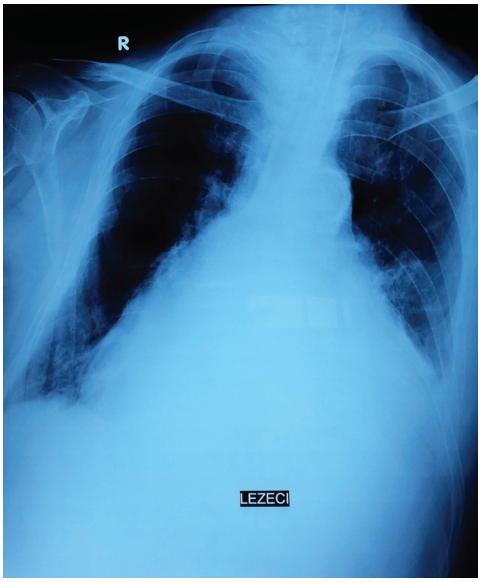

Figure 2. *Control chest X-ray at the admission in ICU.*

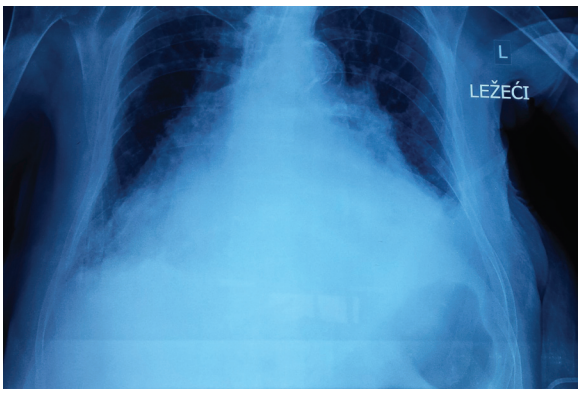

Figure 3. *Control chest X-ray after interval of 6 hours from admission in ICU.*

After that patient was taken to operation theatre and positioned supine. During the treatment patient had a fall of heart rate to 50/min and atropine 0.5mg was adminis-

tered after what heart rate revert to 80/min. There was no oscillation in blood pressure. The total duration of the surgery interventions were approximately 30 min. At the end of treatment patient become somnolent and respiratory insufficient and was intubated with cuffed endotracheal tube 7.5 mm ID (Internal Diameter). She was admitted to ICU and connected to respirator. Until that moment, from admission in hospital (interval of 6 hours), she received 700ml crystalloid solution.

First few hours after admission patient was hemodynamically unstable and continuous norepinephrine infusion was started in the dose required to attain normotension. Later during that day her neurological condition improved, in the evening she regained consciousness and became communicative. Thereafter, she was switched from SIMV mode to CPAP mode of respiration.

We investigated possible causes of such outcome. Since the peripheral nerve block was performed, two control chest X-rays were done (immediately after the surgery when she was admitted in the ICU, and 6 hours later) [Fig. 2 and 3]. A pneumothorax and iatrogenic paresis of phrenic nerve were excluded, and cardiac decompensation as a cause of patient's respiratory insufficiency and somnolence was suspected. Acute congestive heart failure was confirmed by combination of X-ray and increased proBNP 6781 g/L (normal value for patients over 75 years is under 450g/L).

During the next day patient's respiratory function improved and she was disconnected from respirator and extubated. A motor function of the left recovered within 14 hours after the local anesthetic injection. The patient reported that sensory block was present for 4 more hours after that (overall 18 hours). On the day after, she was discharged to surgical ward with normal blood pressure and respiratory function. The later was confirmed by blood gas analysis.

On the same day, in the afternoon, patient was readmitted to ICU because of repeated episode of respiratory insufficiency. Her saturation as measured by pulse oximetry, with 6L of 100% oxygen applied was 82%. She was intubated and assisted ventilation was continued. The control chest X-ray that was done has confirmed repeated congestive heart failure. In the laboratory reports an increased value of CRP (192.1 mg/L) was registered, the rest of findings didn't show any significant deviations. A tracheal aspirate for analysis was taken, and Enterobacter species was confirmed. A specific antibiotic therapy according to antibiogram was started. Despite all supportive measures, her physical condition deteriorated and she died on 19th day of hospitalization.

DISCUSSION

Anesthetic management of patients with cardiomyopathy, with reduced systolic function, is challenging and it may be associated with high mortality. It is commonly complicated by congestive heart failure and malignant arrhythmias. Dilated cardiomyopathy is defined as a deterioration of the function of the myocardium, either caused by left ventricular or biventricular dilatation or due to impaired systolic function of one or both ventricles, with impaired ventricular contractility. The anesthesiologist should have a thorough knowledge on its pathophysiology, clinical features, diagnostic evaluations and the treatment modalities. This has to be accompanied by a careful planning to provide safe anesthesia. Choice of anesthesia should be planned and it should be aimed to reduce hemodynamic fluctuations *(6).* The use of peripheral nerve blocks in the elderly is a rational approach for appropriate surgery as it has minimal influence on hemodynamics *(7).*

All investigation that we took in our patient to define cause of respiratory insufficiency suggested that it was caused by acute congestive heart failure as a complication of severe cardiomyopathy. Our suspicion was supported with the fact that it occurred again shortly after discharge from ICU.

Studies show that overall mortality and morbidity is higher in emergency anesthesia than in elective anesthesia and that ASA physical status correlates with overall mortality and morbidity, regardless of etiology, as well. For the patients with ASA IVE physical status the incidence of all critical events totally attributable to anesthesia is 14.85% and the overall mortality rate totally attributable to anesthesia is 6.60% *(8).*

This case confirms that despite all the measures and precautions that were taken, with choosing anesthesia aimed to reduce haemodynamic fluctuations, with careful planning and balancing hydration of patient, we still may have unwanted complications.

CONCLUSION

The elderly population is the fastest growing part of the population in the developed world. Aging increases the probability of a person to undergo surgery. It alters both pharmacokinetic and pharmacodynamic aspects of anesthetic management *(9).* Anesthesia planning, preoperative assessment, optimizing cardiac status and medical management, formulating the good anesthetic plans and postoperative monitoring, prompt diagnosis and management of complications have to be considered to minimize the incidence of critical events and the mortality rate.

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Paravertebral block: review of the literature

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Abbreviations:
PVB – Paravertebral Block
MeSH – Medical Subject Headings
LA – Local Anesthetic
RCT – Randomised Control Trial
GA – General Anesthesia

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Abstract

Background: *Paravertebral Block (PVB) is an established regional anesthetic technique. It is technically easy to perform and is being used increasingly for intra-operative and post-operative analgesia. This popularity is mainly due to the ease of the technique and fewer complications.*

Materials and Methods: *This is quantitative systematic review of literature database with the aim to assess the efficacy and safety of Paravertebral block in thoracic, abdominal and breast surgery.*

Results: *Six randomised control trials that included 386 patients were reviewed. Authors of reviewed articles reported 100% success in block effectivenes and low incidence of complications.*

Conclusion: *Paravertebral block is effectiv anesthetic/analgetic technique with very few complications*

INTRODUCTION

Paravertebral Block (PVB) is an established regional anesthetic technique. The injection of local anesthetic in a space immediately lateral to where the spinal nerves emerge from the intervertebral foramina produces unilateral, segmental, somatic, and sympathetic nerve blockade which is effective for anesthesia and in treating acute and chronic pain of unilateral origin from the chest and abdomen.

PVBs are highly adaptable and, except for thoracotomy, may serve as the primary anesthetic for breast surgery, chest trauma, hernia repair, soft tissue mass excisions, and /or as a useful adjunct in laparoscopic surgery, cholecystectomy, nephrectomy, or other abdominal and thoracic surgery *(1).*

MATERIAL AND METHODS

The aim of this quantitative systematic review of literature database was to assess the efficacy and safety of PVB in thoracic, abdominal and breast surgery. The systematic search was conducted in the Central register of controlled trials of the Cochrane Library ,MEDLINE and EMBASE according to the current recommendations of the CochraneCollaboration *(2).*The search strategy consisted of a combination of free text words and Medical Subject Headings (MeSH) terms: 'paravertebral', 'thoracic surgery', 'abdomina surgery' and 'breast surgery'

The authors scanned the avaliable articles by the initial search to exclude irrelevant studies.

Study eligibility was determined by reading the title and abstracts and obviously irrelevant trials were excluded at this stage.

The six studies that are included in review are in Table 1 *(3, 4, 5, 6, 7, 8).*

TABLE 1
Studies included in review.

Trial	No of patients	Type of surgery	Type	Details
Naja and colleagues *(3)*	60	Breast surgery	MPVB	Lidocaine 1%, bupivacaine 0.5%, fentanyl, clonidine, epinephrine
Wassef *et al.(4)*	30	Heniorraphy	MPVB	2%lidocain,epinephrin
Klein and colleagues *(5)*	60	Breast surgery	MPVB	Bupivacaine 0.5%, epinephrine
Richardson *et al.(6)*	100	Thoracic surgery	SPVB	0,5% bupivacain
Hadžić *et al (7)*	50	heniorraphy	SPVB	0,75% ropivacain
Pusch and colleagues*(8)*	86	Breast surgery	SPVB	Bupivacaine 0.5%

MPVB – multiple paravertebral block
SPVB – single paravertebral block

RESULTS

The studies included in the reviw were randomised, control trials(RCT).Hadžić, Naja,Pusch and Klein reported 100% success in block effectivenes. The failure rate associated with PVB is not > 9%.Inadvertent vascular puncture (5,2%), hypotension (6%), epidural spread of Local Anesthetic (LA) (1,8%), inadvent pleural punction (1.8%) and pneumothorax (0.5%) were the recorded complications. Complicatins were higher in bilateral compared to unilateral block. Postoperative nausea and vomiting are significantly lower in patients given PVB compared to GA.

DISCUSSION

First PVB was performed in 1905 as an alternative to neuraxial block for obstetric procedures and became a popular technique for the provision of analgesia in the early part of the twentieth century *(9,10).*

The technique however remained neglected till the late 1970s. Renaissance for PVB began 1979 due to efforts from Eason and Wyatt who presented a reappraisal on Thoracic Paravertebral Block (TPVB) *(11).*

PVB is technically easy to learn with a high success rate, and is being used increasingly for not only intra-operative and post-operative analgesia but also as a sole anesthetic technique for carrying out various procedures. This popularity is mainly due to the ease of the technique and fewer complications.

Post-operative pain control is one of the major concerns in the post-operative care of patients undergoing thoracic surgery, especially when thoracotomy is required. In thoracic surgery PVB is placed at the level of the surgical thoracic incision,in most of the cases it is a unilateral block *(12).*

The injection of LA in the paravertebral space produces analgesia because of direct contact of LA with the spinal nerve roots before they emerge from the intervertebral foramina.

The pain associated with thoracotomy surgery can be severe *(13).*

Pain stimuli arising from skin and muscles incision as well as from ribs are spread and conducted by intercostal nerves that are also important for the transition from acute to chronic pain from nociceptive to neurogenic and neurophatic pain.

The paravertebral block has also been used extensively for anaesthesia and analgesia for abdominal surgery, especially for ambulatory inguinal hernia repair *(4, 14).*

The injection of LA into the paravertebral space avoids the severe autonomic dysfunction seen with neuraxial techniques and allows the patient to mobilise earlier.

The paravertebral approach to analgesia after inguinal herniorrhaphy can provide analgesia that is superior to oral analgesia or local field blocks.

Breast surgery under the PVB showed satisfactory pain control with no need for supplementation of analgetics. Postoperative pain is effectively controlled and patients rated the experience as very satisfactory *(15).*

From the retrived papers,with eception of reviwed articles, additinal posibility for PVB application is observed.

Paravertebral blocks have been used less frequently for other abdominal procedures. A series of ten patients undergoing abdominal vascular surgical procedures was reported. Cardiovascular stability was noted upon incision, clamping of the aorta and throughout surgery in all patients *(16).*

No further intra-operative opioids or neuromuscular blocking drugs were required and postoperative analgesia was excellent.

The paravertebral block has also been used successfully as rescue analgesia for visceral pain after failure of

systemic analgesics for renal colic in an obstetric patient. Described experiences with liver surgery-pain control following radiofrequency ablation of liver mass *(17)* as well for percutaneous transhepatic biliary drainage were satisfactory*(18)*.

The effect of PVB examined on the pain-relief and perioperative stress response in patients scheduled for open cholecystectomy showed less pain scores and less requirements on supplemental analgesics for three days postoperatively.A significant reduction in circulatory and hormonal response to stress was also seen *(19)*.

In conclusion, based on the current evidence, PVBs for surgical anesthesia at the level of the thoracic and lumbar vertebrae are associated with less pain during the immediate postoperative period, as well as less postoperative nausea and vomiting, and greater patient satisfaction compared with GA. A modern approach to pain control should consider that reduction or elimination of pain, reduction of morbidity, length of stay and hospital costs.

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PROGRAMME
AND ABSTRACT BOOK

6. HRVATSKI KONGRES REGIONALNE ANESTEZIJE I ANALGEZIJE S MEĐUNARODNIM SUDJELOVANJEM

6TH CROATIAN CONGRESS OF REGIONAL ANAESTHESIA AND ANALGESIA WITH INTERNATIONAL PARTICIPATION

Croatian Society of Regional Anaesthesia and Analgesia
Croatian Medical Association

European Society of Regional Anaesthesia

Hotel DUBROVNIK, Zagreb, Croatia
June 12–13, 2015

www.hdraa.com.hr

Organizers:

Croatian Society of Regional Anaesthesia and Analgesia-Croatian Medical Association (CSRAA-CroMA)
European Society of Regional Anaesthesia & Pain Therapy (ESRA)
Josip Juraj Strossmayer University of Osijek, Faculty of Medicine

Under the Auspices of:

Department of Medical Sciences, Croatian Academy of Sciences and Arts

Organizing committee presidents:

K. Šakić (Croatia), M. Van de Velde (Belgium)

Scientific committee:

J. De Andrés (Spain), V. Paver Eržen (Slovenia), S. Gligorijevic (Switzerland), K. Šakić (Croatia), M. Van de Velde (Belgium)

CONGRESS PROGRAMME

DAY 1: FRIDAY, June 12, 2015
HALL Ban Josip Jelačić, Hotel Dubrovnik

12:00 –	**REGISTRATION**
	Registration desk
14:30 – 18:30	**SESSION 1** **HIGHLIGHTS IN REGIONAL ANAESTHESIA & PAIN MEDICINE** *Chair: J. De Andrés (Spain), S. Gligorijevic (Switzerland)*
14:30 – 15:00	**Genetics and pain** *D. Primorac, Zagreb, Croatia*
15:00 – 15:30	**Pain medicine - medical management of acute and chronic pain** *J. De Andrés, Valencia, Spain*
15:30 – 16:00	**POSTER PRESENTATIONS** *Chair: V. Nesek Adam (Zagreb), D. Bandić Pavlović (Zagreb), J. Pavičić Šarić (Zagreb)*
15:30 – 16:00	**Coffee break**
16:00 – 16:30	**Status of Regional anesthesia & Pain medicine in undergraduate and postgraduate study – today and tomorrow** *M. Van de Velde, Leuven, Belgium*
16:30 – 17:00	**What is new in Education and Teaching in Regional anaesthesia?** *V. Paver Eržen, Ljubljana, Slovenia*
17:00 – 17:30	**Adverse events and regional anaesthesia: Preventing the preventable** *S. Gligorijevic, Zuerich, Switzerland*
17:30 – 18:00	**Spinal anaesthesia and stress response in hip trauma** *K. Šakić, Zagreb, Croatia*
18:00 – 18:30	**Discussion**
20:00 – 22:00	**WELCOME RECEPTION, Hotel Dubrovnik, 1st floor**
	CSRAA 2015 Best Poster Award
	Musical act: M. Barišin and Pavao Markovac, Music School String Quintet

DAY 2: SATURDAY, June 13, 2015
HALL Ban Josip Jelačić, Hotel Dubrovnik

08:00 – 10:30	**SYMPOSIUM I** **REGIONAL ANAESTHESIA AND ANALGESIA** *Chair: M. Van de Velde (Belgium), K. Šakić (Croatia)*
08:00 – 08:40	**Update in obstetric Regional Anesthesia** **Anesthetic management of the severly preeclamptic parturient** *M. Van de Velde, Leuven, Belgium*
08:40 – 09:10	**Perioperative Analgesia for thoracic surgery** *V. Novak Jankovič, Ljubljana, Slovenia*

09:10 – 09:40	**Update in orthopaedic Regional Anesthesia: state of the art practice** *B. Tripković, Zagreb, Croatia*
09:40 – 10:10	**Ultrasound use for nerve blocks and management strategies in outpatient surgery** *K. Oremuš, Zagreb, Croatia*
10:10 – 10:30	**Discussion**
10:30 – 11:00	**POSTER PRESENTATIONS** *Chair: Chair: S. Kvolik (Osijek), J. Peršec (Zagreb)*
10:30 – 11:00	**Coffee break**
11:00 – 13:00	**SYMPOSIUM II** **PAIN MEDICINE** *Chair: J. De Andrés (Spain), I. Radoš (Croatia)*
11:00 – 11:20	**Anatomy and Physiology of nociception and centrally-mediated pain states** *Z. Petanjek, Zagreb, Croatia*
11:20 – 12:00	**Invasive procedures for chronic pain** *J De Andrés, Valencia, Spain*
12:00 – 12:20	**Neurosurgical procedures for chronic pain treatment** *D. Chudy, Zagreb, Croatia*
12:20 – 12:40	**Postoperative Neurological Sequelae – Management, early Diagnosis and treatment of Neurologic complications after regional anaesthesia** *V. Bašić Kes, Zagreb, Croatia*
12:40 – 13:00	**Discussion**
13:00 – 14:00	**Lunch break** *Hotel restaurant*
14:00 – 16:00	**SYMPOSIUM III** **CLINICAL RESEARCH IN REGIONAL ANAESTHESIA** *Chair: D. Tonković (Croatia), S. Kvolik (Croatia)*
14:00 – 14:20	**Effect of age on onset time and duration of sensory blockade in regional anaesthesia** *J. Pavičić Šarić, Zagreb, Croatia*
14:20 – 14:40	**Attenuation of systemic inflammatory stress response after preoperative analgesia with clonidine compared to levobupivacaine** *J. Peršec, Zagreb, Croatia*
14:40 – 15:00	**Upper extremity blocks or general anaesthesia** *S. Baranović, Zagreb, Croatia*
15:00 – 15:20	**Paravertebral blocks in high risk thoracic surgery** *J. Špiček Macan, Zagreb, Croatia*
15:20 – 15:40	**Neuropathic Orofacial pain – diagnostic and therapeutic challenges** I. *Šklebar, Zagreb, Croatia*
15:40 – 16:00	**Discussion**
16:00 – 16:30	**POSTER PRESENTATIONS (P17–P24)** *Chair: V. Golubović (Rijeka), T. Šimurina (Zadar), L. Kalagac Fabris (Pula)*
16:00 – 16:30	**Coffee break**
16:30 – 17:30	**SYMPOSIUM IV** **MISCELLANEOUS TOPICS IN REGIONAL ANAESTHESIA** *Chair: I. Suljević (Bosnia and Herzegovina), V. Nesek Adam (Croatia)*

16:30 – 16:45	**Anaesthetic procedures and pain relief for child delivery in Bosnia and Herzegovina** *I. Suljević, Sarajevo, BIH*
16:45 – 17:00	**Regional anesthesia in cancer surgery: update** G. *Brozović, Zagreb, Croatia*
17:00 – 17:15	**Perioperative pain management in ICU patients** *V.Nesek Adam, Zagreb, Croatia*
17:15 – 17:30	**Regional anesthesia in children: indications and limitations** *A. Hasani, Pristhina, Kosovo*
17:30 – 17:45	**Radiofrequency denervation of lumbar facet joints in the treatment of chronic low back pain** *I. Radoš, Osijek, Croatia*
17:40 – 18:20	WORKSHOPS – PART 1
Hall A	**W 01 Nerve location for peripheral nerve blocks: ultrasound and nerve stimulation** **Upper extremity blocks**
	Brachial plexus – Proximal approaches: interscalene, infraclavicular **Distal approaches: nerve blocks at elbow and wrist level** *Demonstrators/speakers: K. Oremuš, Croatia*
Hall B	**W 02 Nerve location for peripheral nerve blocks: ultrasound and nerve stimulation** Lower extremity blocks
	Proximal approaches: psoas compartment, femoral and sciatic nerve blocks. **Distal nerve blocks: sciatic and saphenous nerve block at the knee and ankle level** *Demonstrators/speakers: S. Huterer, Austria*
Hall C	**W 03 Paravertebral, sympathetic, and other blocks**
	Demonstrators/speakers: J. Ažman, I. Skok, Croatia
Hall D	**W 04 Airway management, Topical anaesthesia of the airway** Ganglion stelatum block Sympathetic block, and other blocks
	Demonstrators/speakers: V. Frković, T. Goranović, Croatia
18:20 – 19:00	WORKSHOPS – PART 2
Hall A	**W 01 Nerve location for peripheral nerve blocks: ultrasound and nerve stimulation** **Upper extremity blocks**
	Brachial plexus - Proximal approaches: interscalene, infraclavicular Distal approaches: nerve blocks at elbow and wrist level *Demonstrators/speakers: K. Oremuš, Croatia*
Hall B	**W 02 Nerve location for peripheral nerve blocks: ultrasound and nerve stimulation** **Lower extremity blocks**
	Proximal approaches: psoas compartment, femoral and sciatic nerve blocks. **Distal nerve blocks: sciatic and saphenous nerve block at the knee and ankle level** *Demonstrators/speakers: S. Huterer, Austria*
Hall C	**W 03 Sympathetic trunk (Ganglion stelatum, plexus celiacus and other blocks)**
	Demonstrators/speakers: J. Ažman, I. Skok, Croatia
Hall D	**W 04 Airway management, Topical anaesthesia and upper airway blocks** **Paravertebral and other blocks**
	Demonstrators/speakers: V. Frković, T. Goranović, Croatia
19:10 – 21:00	CLOSING CEREMONY

POSTER PRESENTATION SCHEDULE

FRIDAY, June 12, 2015

15:30 – 16:00 **POSTER PRESENTATIONS (P 1 – P8)**
D. Bandić Pavlović(Zagreb), J. Pavičić Šarić (Zagreb)

P 1 PATIENTS' SATISFACTION WITH SPINAL ANESTHESIA IN PATIENTS UNDERGOING INGUINAL HERNIA REPAIR
Daniela Bandić Pavlović, Sanja Sakan, Željka Martinović, Igor Virag, Klaudija Prlić, Dinko Tonković, Mladen Perić

P 2 FACTORS ASSOCIATED WITH SUCCESSFUL PERFORMANCE OF UNILATERAL SPINAL ANESTHESIA FOR VARICOSE VEIN SURGERY
Kristina Medved, Damira Vukičević, Marko Oreški

P 3 INFLUENCE OF UNILATERAL SPINAL BLOCK ON HAEMODYNAMIC PROFILE IN DIABETIC AND NON-DIABETIC PATIENTS
Petra Ožegović, Vanja Vončina, Jelena Zenko, Jadranka Pavičić Šarić

P 4 SPINAL ANAESTHESIA AND IT´S COMPLICATIONS – EVALUATION OF EXPECTATIONS, IMPRESSIONS AND EXPERIENCES AMONG PATIENTS
Sonja Krofak, Višnja Nesek Adam, Petra Matković, Maja Karaman – Ilić, Žarko Rašić, Livija Šakić

P 5 EPIDURAL ANESTHESIA IN PATIENT WITH DBS – OUR FIRST CASE
Marin Knez, Nikolina Narančić Knez, Ante Tolić, Marina Nekić Borčilo, Alfio Poropat, Milica Komšo, Anamarija Mrđen, Orijana Džepina

P 6 SPINAL ANESTHESIA FOR LUMBAR SPINE SURGERY IN UNIVERSITY CLINICAL HOSPITAL MOSTAR
Dajana Vladić, Mirko Mihalj, Anita Kosjerina, Zoran Karlović, Vesna Golubović

P 7 SUPRACLAVICULAR NERVE BLOCK: DOES KIDNEY TRANSPLANTATION MAKE A DIFFERENCE?
Katarina Tomulić Brusich, Ivana Acan, Vesna Kovačić Vicić, Nataša Višković Filipčić

P 8 ULTRASOUND-GUIDED TRANSVERSUS ABDOMINIS PLANE BLOCK IN COMBINATION WITH ILIOINGUINAL AND ILIOHYPOGASTRIC BLOCK IN A HIGH RISK CARDIAC PATIENT FOR INGUINAL HERNIA REPAIR: A CASE REPORT
Stjepan Barišin, Viktor Đuzel, Livija Šakić

SATURDAY, June 13, 2015

10:30 – 11:00 **POSTER PRESENTATIONS (P 9 – P 16)**
Chair: I. Matić (Slavonski Brod), J. Peršec (Zagreb), I. Škeblar (Zagreb)

P 9 ARTERIAL PRESSURE AND HEART RATE CHANGES IN PATIENTS DURING „BEACH CHAIR POSITION" FOR SHOULDER SURGERY: COMPARISON OF THE REGIONAL AND GENERAL ANESTHESIA TECHNIQUES
Ivana Haršanji Drenjančević, Domagoj Drenjančević, Danijela Gulam, Slavica Kvolik, Tomislav Ružman, Gordana Kristek

P 10 FEMORAL NERVE BLOCK IN A HIGH RISK CARDIAC PATIENT. CASE REPORT.
Verica Mikecin, Miroslav Župčić, Sandra Graf Župčić, Sanja Peremin, Viktor Đuzel, Ana Briški, Ino Husedžinović

P 11 THE USE OF AN ULTRASOUND-GUIDED SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK IN A HIGH RISK PATIENT WITH CARDIOMYOPATHY
Barbara Palković, Ivana Haršanji Drenjančević, Dubravka Ivić, Slavica Kvolik

P 12 COMPARISON OF MINIMUM EFFECTIVE VOLUME OF LOCAL ANESTHETIC FOR ULTRASOUND GUIDED SUPRACLAVICULAR BLOCK ($MEAV_{95}$) IN ELDERLY AND MIDDLE AGED PATIENTS
Jadranka Pavičić Šarić, Vinko Vidjak, Jelena Zenko, Matea Bogdanović Dvorščak, Vanja Vončina, Nataša Paklar

P 13 SCALP BLOCK FOR HEMODYNAMIC STABILITY DURING NEUROSURGERY
Dinko Tonković, Vasilije Stambolija, Marin Lozić, Petar Martinović, Daniela Bandić Pavlović, Ante Sekulić, Robert Baronica, Mladen Perić

P 14 PARAVERTEBRAL BLOCK: REVIEW OF LITERATURE
Maja Karaman – Ilić, Višnja Nesek Adam, Martina Matolić, Jana Kogler, Dijana Butković

P 15 THE APPLICATION OF PARAVERTEBRAL BLOCK IN HIGH-RISK PATIENTS WITH CARDIORESPIRATORY, LIVER AND KIDNEY PROBLEMS: A CASE REPORT
Miroslav Župčić, Sandra Graf Župčić, Ana Brundula, Iva Korečić Zrinšćak, Jasminka Peršec, Ino Husedžinović

P 16 TRENDS IN OBSTETRIC REGIONAL ANESTHESIA AND ANALGESIA AT SVETI DUH UNIVERSITY HOSPITAL
Ivan Šklebar, Tino Klancir, Livija Šakić, Luka Djulabić

16:00 – 16:30 **POSTER PRESENTATIONS (P 17 – P 24)**
Chair: V. Golubović (Rijeka), T. Šimurina (Zadar), L. Kalagac Fabris

P 17 SATISFACTION WITH REGIONAL ANESTHESIA IN PARTURIENTS UNDERGONE CAESAREAN SECTION
Sonja Škiljić, Dubravka Ivić, Gordana Kristek

P 18 PATIENT SATISFACTION WITH REGIONAL ANESTHESIA IN ORTHOPEDIC SURGERY
Tomislav Ružman, Nataša Ružman, Ivana Haršanji Drenjančević, Gordana Kristek, Danijela Gulam, Slavica Kvolik

P 19 INFLUENCE OF DEXAMETHASONE ADMINISTRATION IN SPINAL ANESTHESIA FOR FEMUR FRACTURE ON POSTOPERATIVE COGNITIVE DYSFUNCTION
Livija Šakić, Dinko Tonković, Borna Josip Godan, Katarina Šakić

P 20 LUMBAR SPINAL STENOSIS: METHODS OF TREATMENT WITH EMPHASIS ON EPIDURAL STEROID INJECTIONS
Neven Elezović, Dragica Kopić, Sanda Stojanovic Stipić, Ana Šarić, Anela Elezović, Tomislav Ljubičić

P 21 PROLONGED RELIEF OF HEAD AND FACE NEURALGIA AFTER REGIONAL NERVE BLOCKS
Lada Kalagac Fabris, Maša Biberić

P 22 TEMPOROMANDIBULAR JOINT DISORDER AND HEADACHE – ONE-YEAR-FOLLOW-UP
Iva Klarić, Tomislav Badel, Vanja Bašić Kes, Samir Ćimić, Dijana Zadravec

P 23 LOCAL ANALGESIA IN PAIN MANAGEMENT AFTER CARDIAC SURGERY
Anita Kosjerina, Zoran Karlović, Vesna Golubović, Dajana Vladić

P 24 DOES ROTATION THROMBELASTOMETRY (ROTEM®) IMPROVE EARLY PREDICTION OF COAGULOPATHY IN (BENIGN AND MALIGNANT) BREAST TUMOR?
Dinko Bagatin, Katarina Šakić, Tomica Bagatin, Deana Šturm, Milan Milošević

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Abstracts

A1, P1: Patients' satisfaction with spinal anesthesia in patients undergoing inguinal hernia repair

DANIELA BANDIC PAVLOVIC[1], SANJA SAKAN[2], ZELJKA MARTINOVIC[3], IGOR VIRAG[2], KLAUDIJA PRLIC[2], DINKO TONKOVIC[1], MLADEN PERIC[1]

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Background and goal: The aim of the study was to assess patients satisfaction, postoperative complication and hospital stay with SA.

Materials and methods: This observational, retrospective study included 27 patients in Clinical hospital center Zagreb in six months period. Patients were interviewed by phone for satisfaction by Likert scale from one (very unsatisfied) to five (very satisfied) for anesthesia, for pain by VAS (1 to 10), presence of PONV, headache and urinary retention. Following data were collected from medical documentation (age, sex, BMI, ASA, hospital stay).

Results: In spinal group median age was 65 years (range 23-82), BMI was normal in 17 patients and increased in 10 patients, 18 patients were ASA 1 and 2, seven were ASA 3 and 2 were ASA 4. From complication, two patients had a headache, two vomiting and five patients had urinary retention. 20 patients assess satisfaction with anesthesia in spinal group as very satisfied, 3 as satisfied, 1 as neutral, 1 as unsatisfied and 2 as very unsatisfied. Satisfaction in postoperative period of this group was as follows: 13 were very satisfied, 10 were satisfied, 1 was neutral, nobody was unsatisfied and 3 were very unsatisfied. All four patients marked their satisfaction as unsatisfied or very unsatisfied due to development of urinary retention. Median of hospital stay was three days.

Conclusion: From patients point of view, for scheduled inguinal hernia repair high degree of satisfaction provides SA. While urinary retention was the reason of patients' unsatisfaction, other complication patients have not been related with dissatisfaction.

A2, P2: Factors associated with successful performance of unilateral spinal anesthesia for varicose vein surgery

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Background and purpose: Unilateral spinal anesthesia provides excellent surgical anesthesia and postoperative analgesia with minimal effect on motor limb blockade. This enhances patient recovery and hospital discharge. Single center retrospective study was conducted to determine factors associated with unilateral spinal block performance.

Materials and methods: Medical records of patient undergoing varicose vein surgery at University Hospital Merkur, between February 2014 and February 2015 were reviewed. All patients underwent unilateral spinal anesthesia with hyperbaric anesthetic solution (0.5% levobupivacaine 10 mg, fentanyl 25 mg and 0.5 mL of 40% glucose). Patients were divided according to age (young <35 years, mean 35-65 years, older >65 years), body mass index (BMI kg/m^2; <25, 25-30, >30) and presence of musculoskeletal system pathology.

Results: A total of 97 patients gave written consent for unilateral spinal block performance - 35 males (36.1%) and 62 females (63.9%). Successful rate performance for surgical anesthesia was 86.6%. Thirteen patients (13.4 %) had to be converted to general anesthesia. Patient factors were analyzed using linear regression model. Failure of adequate anesthesia was not associated with age ($p < 0.05$) and BMI ($p < 0.05$). However, presence of musculoskeletal lumbar pathology had significant impact on the unilateral spinal block success ($p < 0.01$).

Conclusion: Failure of unilateral spinal anesthesia is associated with musculoskeletal lumbar pathology and not with age or BMI.

A3, P3: Influence of unilateral spinal block on haemodynamic profile in diabetic and non-diabetic patients

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Background and purpose: Patients with diabetes mellitus (DM) are at higher risks of haemodynamic instability during anaesthetic procedures, including spinal anaesthesia. A hyperbaric solution of local anaesthetics (LA) for spinal anaesthesia allows for a reduction in dose, hence decreasing side effects while ensuring an adequate sensory block. We analyzed hypotension following the establishment of unilateral block in two groups of patients, diabetic and non-diabetic.

Materials and methods: In our retrospective clinical study we collected data for 44 patients who underwent lower limb surgery, 22 diabetic and 22 non-diabetic. Patients were comparable in terms of age, ASA status, pre-procedural volume therapy, premedication and dose of administered LA. Following a successful unilateral spinal block, arterial blood pressure (BP) was measured every 5 minutes during surgical procedure. The lowest BP in the first 30 minutes was taken in calculation. Administration of vasoactive drugs was noted.

Results: Even though both systolic and median arterial pressure on average decreased more in the diabetic group than in the non-diabetic (23.6 % versus 21.9 and 24.2 versus 20.7, respectively) none of these differences were statistically significant. Furthermore, only two diabetic patients had hypotension that warranted administration of vasopressors, but the occurrence of such clinically relevant hypotension was not statistically significantly different from the non-diabetic group.

Conclusion: Our results showed no difference in hypotension in diabetic patients compared to non-diabetic patients. Therefore, unilateral block with low doses of local anesthetic is a safe form of anesthesia that guarantees haemodynamic stability even in such a distinctive group of patients.

A4, P4: Spinal anaesthesia and it's complications – evaluation of expectations, impressions and experiences among patients

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Background and purpose: Every surgical procedure, together with anaesthesia is stressful for a patient. In order to introduce patients' personal impressions of spinal anaesthesia, our aim was to analyse their expectations, fears and other emotions. We compared those emotions to objective measures to estimate the success of spinal anaesthesia.

Materials and methods: Prospective study included 30 patients aged 18 – 65, ASA I - III status, who are native or proficient in Croatian language and are undergoing an elective surgical procedure. Exclusion criteria were patient´s refusal, allergy to local anaesthetics, coagulopathy, severe spine deformation, failed or inadequate spinal block, history of alcohol or narcotic abuse, and psychiatric history. We developed our own structural questionnaire in order to investigate patient's emotions before spinal anaesthesia performance and during the operation itself and the day after. It contained 33 questions based on Likert´s method. As objective measures to estimate the success of spinal anaesthesia, we focused on providing a regional block in an expected time and presence of complications and side-effects of spinal anaesthesia.

Results and conclusion: Although our questionnaire hasn`t been validated, it helped us to understand the dominating emotions among patients undergoing spinal anaesthesia and to recognize the connection between patient´s personal expectations and objective outcome of spinal anaesthesia experience. Total patient satisfaction with spinal anaesthesia and willingness to undergo an operation in spinal anaesthesia again if neccessary, were more expressive among patients who showed positive emotions before spinal anaesthesia performance. Since this research showed some interesting trends, a space for further questions and upgrading the research opened.

A5, P5: Epidural anesthesia in patient with deep brain stimulation – our first case

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We present a case of a 69-year-old male patient with an essential tremor and deep brain stimulator (DBS) implanted in his left thalamus 2 years ago in Department of Neurosurgery, University hospital Dubrava, Zagreb.

The patient's left leg has been amputated after war trauma and TEP implanted in his right knee. He has oesophagitis of Barret, chronic prostatitis, and underwent surgery of baseocellular carcinoma of face and lumbar spine stenosis. Both procedures were before DBS implantation. Last year in May he had surgery in general anesthesia of chronic dacrocystitis of left eye. After that the twitches (jerks) of the head and left arm appeared and were characterized as thalamic bursts in thalamic stimulated patient.

Now, the same patient needs a surgery of right knee because of gonarthrosis and he needs implantation of reTEP. Team of medical specialist (neurologist, cardiolologist and anesthesiologist) made preoperative examinations. In neurological status patient had tremor of both hands, more in left one. Our cardiologist needed to make heart ultrasound; she could not make ECG regularly because of DBS. Preoperative laboratory findings of blood and urine and X-ray of heart and chest were normal.

Because of the side effects after general anesthesia during surgery few months ago, our anesthesiologist decided to make this operation in epidural anesthesia. They were not able to switch off DBS before surgery.

Before surgery, anesthesiologist inserted epidural catheter between L2 and L3 vertebra and applicated mixture of local anesthetic 0.5% levobupivacaine (10 ml) and fentanyl (1ml) diluted in saline in 1:1 ratio, in 3 boluses of 5 ml, total 15 ml. After that he applicated another bolus of 5 ml just before the end of surgery. During the surgery patient was haemodinamic stable, with normal vital functions and partly preserved motor skills of legs.

After the procedure we continued with epidural analgesia (the same mixture in lower ratio) without using other analgesics. Patient didn't have new neurological symptoms and he felt good. Sixth day after the surgery he was transfered in Department of physical therapy.

A6, P6: Spinal anesthesia for lumbar spine surgery in University Clinical Hospital Mostar

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Until 2012 in the University Clinical Hospital (UCH) Mostar lumbar spine surgical procedures were performed in general anesthesia using standard anesthetic procedure. The first lumbar spine surgery under spinal or subarahnoidal anesthesia was performed on the 23rd of May 2012. Since then spinal anesthesia for lumbar spine surgery was considered as a standard anesthetic technique in UCH Mostar.

The mixture of anesthetic drugs was applied in subarachnoidal space two intervertebral spaces above the intervertebral space that was planned to be operated. Considering the needed distance between the punctated intervertebral space and planned operative field, spinal anesthesia for lumbar spine surgery can be applied only for surgery from fourth lumbar vertebra bellow. In UCH Mostar, we use it for L4/L5 and L5/S1 discectomies. Spinal puncture is performed with the spinal needles with smallest diameter that are available (25-27 Gauge) in sitting or lateral decubitus position. The mixture of local anesthetic levobupivacaine 0.5% (cca 2 ml) and opioid drug fentanyl (cca 2,5 mcg) was injected in spinal space and the patient was turned in supine position. After clinical confirmation that applied anesthetic mixture has reached adequate space, the patient was rolled in prone position adequate for the planned surgery.

Since May of 2012 we have started performing spinal anesthesia for lumbar spine surgery, applying the mixture of local anesthetic and opioid drugs. The same year 23 patients were operated in spinal anesthesia and 128 patients underwent general anesthesia. In the year 2013, 59 patients underwent lumbar spine surgery in spinal anesthesia, and 83 patients received general anesthesia. In 2014, 61 patients were operated in spinal anesthesia comparing to 78 patients operated in general anesthesia. Our aim is to improve the quality of anesthetic procedure in our hospital according to ESRA guidelines regarding as well patients' satisfaction and wellbeing during perioperative procedure and hospital stay.

A7, P7: Supraclavicular nerve block: does kidney transplantation make a difference?

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Background and purpose: Number of transplanted patients increased overall. However, clinical research among these patients regarding regional anesthesia is insufficient. Transplanted patients often require upper extremity surgery. Peripheral nerve blocks became popular anesthetic option due to hemodynamic stability and better postoperative analgesia. Single center retrospective study was conducted to determine possible difference among renal transplant patients and non-transplanted patients regarding block onset and duration for supraclavicular nerve block (SCB) where the same dose of local anesthetic was used.

Materials and methods: Medical records of patients with SCB performed for surgical procedures on upper extremities at University Hospital Merkur, between May 2009 and March 2013 were reviewed. All SCB performed were ultrasound-guided. Patients in whom a single-injection of local anesthetic (equal aliquots of lidocaine 2% and levobupivacaine 0.5%) was performed for SCB were included in study. Patients were divided in groups: renal transplant recipients (Tx) and non-transplanted (Non-Tx) patients.

Results: A total of 57 SCB procedures were performed using lidocaine+levobupivacaine mixture: Tx (n=15) and Non-Tx (n=42). Non-Tx patients were older (Tx 51.60+/-9.63 vs Non-Tx 61.45+/-13.19, P=0.0106). However, there was no difference regarding sex, ASA status, patient co-morbidities (diabetes mellitus and coronary artery disease). Tx group had higher body mass index (Tx 32.4+/-6.18 vs. Non-Tx 25.8+/-4.50, P<0.0001). This did not affect block success. There was no difference between total volume of local anesthetic used, time of block onset and block duration.

Conclusion: There is no difference in duration of SCB in patients after kidney transplantation compared to the general surgical population.

A8, P10: Femoral nerve block in a high risk cardiac patient. Case report.

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Background and purpose: Elderly patients admitted to the emergency department usually have concomitant diseases. In risk evaluation for surgery and anesthesia, they usually represent a high risk group. General anesthesia itself could have a deleterious effect on hemodynamic stability so regional techniques are usually preferred in this group of patients.

Case report: We present a case of a 69 year old gentleman admitted to hospital with traumatic rupture of the quadriceps muscle. In preoperative evaluation it was established that he suffers from coronary artery disease, dilative cardiomyopathy, hypothyroidism, hypertension and diabetes mellitus. Due to ASA IV status and high risk of perioperative cardiac complications, it was decided to apply an ultrasound guided femoral nerve block technique combined with the use of a nerve stimulator. A complete sensory block was achieved and the patient was hemodynamically stable during and after the surgical intervention.

Conclusion: Peripheral nerve block is safe and effective in high risk patients with no negative effects on hemodynamic stability. A combined nerve stimulator technique with ultrasound guided femoral nerve block eliminates the need for adjunctive analgesics.

A9, P16: Trends in obstetric regional anesthesia and analgesia at Sveti Duh University Hospital

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Background and purpose: Regional anesthesia and analgesia are the preferred anaesthetic methods recommended for obstetrics. This research examines the frequency and quality of spinal and epidural anesthesia and analgesia used during labor and cesarean section in the six year period from 2009 to 2014 at Sveti Duh University Hospital in Zagreb. Quality is assessed according to the frequency of severe post-dural puncture headache (PDPH), the most common serious complication of central regional blocks.

Materials and methods: A retrospective analysis of obstetric anesthetic management for the past six years was conducted using archived hospital records. Use of a blood patch was considered an indicator for the development of severe PDPH.

Results: In accordance with the falling birth rates throughout Croatia, the number of births at Sveti Duh hospital decreased during the observation period. The use of epidural analgesia for labor increased during the same time period. The rate of cesarean sections remained constant at 19-20% of deliveries. The number of cesarean sections performed under spinal and epidural anesthesia increased along with a concurrent decrease in the use of general anesthesia. The use of a blood patch, indicating the development of severe PDPH, dropped from 27 in 2009 to six in 2013 and 2014. This can be attributed to the transition to thin, atraumatic spinal needles for spinal blocks along with the increased level of experience of the obstetric anesthesiology team.

Conclusions: During the past six years, there was an increasing proportion of births using regional analgesia for labor and regional anesthesia for caesarean sections. Meanwhile, PDPH has been drastically reduced.

A10, P17: Satisfaction with regional anesthesia in parturients undergone caesarean section

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Background and purpose: Regional (RA) and general (GA) anesthesia are used for caesarean sections (CS). Reducing the frequency of GA may serve to reduce maternal complications. Important component of quality of perioperative care is patient's satisfaction with anesthesia service. We investigated the level of satisfaction with anesthetic technique in parturients undergone CS and determined factors influencing on it.

Patients and methods: Retrospective survey was conducted by anonymous questionnaire introduced to parturients undergone CS.

Results: Forty-five women participated. Under RA was done 57.8% of CS (64.7% of electives and 36.4% of urgents). Most parturients had previous information about anesthetic techniques and 79.4% of them participated in choosing the type of anesthesia. High satisfaction with RA revealed 77.8%, while 11.1% of them revealed poor satisfaction, related to patchy-block and conversion to GA. All parturients experienced RA, as well as the ones under GA, would choose the same technique again.

Conclusion: More than 50% elective procedures were done in RA while in urgent cases dominates GA. Parturients were well informed about anesthetic techniques, mostly by internet and anesthesiologist. Reason for RA was possibility of seeing their newborn and for GA fear of awareness. Women who were previously informed, prepaired and participated in choosing the type of anesthesia, showed high level of satisfaction. The patient's previous knowledge as well as participation and approach of anesthesiologist can influence strongly on choice of anesthetic technique and the level of satisfaction with anesthesia in parturients undergone CS.

A11: The comparison of analgesic effect of fractionated and continuous epidural analgesia with painless childbirth during the first stage of labor

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Background: In this study we point out the difference between the analgesic effect of administered local anesthetic and the analgesic epidural block through the techniques of fractionated applications of analgesia and applications of analgesia with continuous infusion technique, in primiparas during the first stage of labor.

Methods: In group G-I, (n-20) local anesthetic and analgesic techniques were applied with fractional epidural block. In group G-II, (n-20) the maintenance of epidural block was administered through the application of infusion. For the test application of 3 ml in both groups we used a mixture of Chirocaine 0.25% 20 ml and 100 mcg Fentanyl. In group G-I, 5 minutes after the application of the test dose there was an application of an additional 7 ml of the same mixture as analgesic dose. In group G-II, after the application of the test dose, an additional dose of 7 ml of a mixture of an analgesic, the continuous analgesia was maintained at a dose of 10 ml / h of the mixture of 0.125% Chirocaine and 1.5 micrograms / ml of fentanyl using Infusomats. Using the VAS scale for pain, the pain was determined before the application test dose and at the end of the first stage of labor.

Results: The average pain intensity before applying the test dose in group G-I was 2.8, and 3.3 in group G-II. At the end of the first stage of labor, at the maximum dilatation of the cervix in group G-I, pain intensity was 2.1, and 4.3 in group G-II.

Conclusion: Epidural analgesia with the application of fractional technique is a more favorable option for the reduction of pain in pregnant women than the continuous infusion.

A12, P21: Prolonged relief of head and face neuralgia after regional nerve blocks

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Background and purpose: The main sensory innervation of the face derives from the cranial nerve V and the upper cervical nerves. Atypical neuralgia is caracterized by unilateral, prominent, constant and severe aching, boring or burning pain within the affected distribution of the cranial nerve.

Patients and methods: 11 patients (7 females/4 males) with facial neuropathic pain (tirgeminal, occipital, frontal-supratrochlear) were forwarded to pain clinic because of complications and side effects of high doses of anticonvulsant and antidepressants therapy but still suffering of severe burning pain. All patients, after they signed informed consents, were treated with three or four series of minimal invasive techniques of reaching the trigeminal/maxillar/cranial nerves through the face without the skin incision. The goal of peripheral levobupivacaine and corticosteroids injections was to block the area of the injured nerves to keep it from sending pain signals to the brain.

Results: All patients experienced an initial total relief of ongoing pain for 8-12 hours. Evoked pain (hyperalgesia or allodynia) was blocked simultaneusly with the spontaneus pain. In all of the patients we achieved a long term decrease of anticonvulsant daily therapeutic doses. In one young female patient with trigeminal (V2) neuralgia the nerve blocks reduced the incidence of pain apareance but she expressed the side effects of corticosteroids injections, so after applying the bocks twice she gave up.

Conclusions: Prolonged relief of neuralgia after regional blocks my be the result of a central action of local anesthetics and corticosteroids at the spinal level after an intra-axonal incorporation and centripetal axoplasmatic transport, and allow us to avoid the drug abuse.

A13, P23: Local analgesia in pain management after cardiac surgery

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Background: Patiens submitted to cardiac surgery under general anesthesia have a lengthened post-operative use of mechanical ventilation, slower recovery, and a longer stay in the Intensive Care Unit (ICU), and have the need for more analgetics after the operation. Infusion of levobupivacaine 0.5%, at the median sternotomy site, for 36 h after cardiac surgery reduces the need for intravenous opioid analgesics and improves the recovery process.

Material and methods: Forty-three consenting clinical trial patients undergoing open-heart surgery with a standardized general anesthetic technique had two indwelling infusion catheters placed at the median sternotomy incision site at the end of surgery. The patients were randomly assigned to receive 1st group opioid analgetics intravenous and 2nd group levobupivacaine 0.5% via an elastomeric infusion pump at the rate of 2-6 ml/h for 36 hours. The patients evaluated their chest pain using the Visual Analog Scale (VAS). The VAS were in 1st group (>3), in levobupivacaine group (=<3).

Results: Compared with the control group, there was a statistically significant reduction in VAS scores in the levobupivacaine group, and they need less opioid analgetics later. Patient satisfaction with their pain management was also improved in the levobupivacaine group.

Conclusion: A continuous infusion of levobupivacaine 0.5% through infusion catheters was effective for pain management, faster weaning from mechanical ventilation, the reduction of stay in the ICU and decreasing the need for opioid analgesic medication.

AUTHORS' INDEX (Posters and Abstracts)

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