



General and Supportive Care

The Dutch national guideline on metastases and hematological malignancies localized within the spine; a multidisciplinary collaboration towards timely and proactive management



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ABSTRACT

Here, we describe the development of a Dutch national guideline on metastases and hematological malignancies localized within the spine. The aim was to create a comprehensive guideline focusing on proactive management of these diseases, enabling healthcare professionals to weigh patient perspectives, life expectancy, and expected outcomes to make informed treatment recommendations. A national multidisciplinary panel consisting of clinicians, a nurse, a patient advocate, an epidemiologist, and a methodologist drafted the guideline. The important role of patients in the realization of the guideline enabled us to identify and address perceived shortcomings in patient care. The guideline covers not only metastatic epidural spinal cord compression, but also the treatment of uncomplicated metastases and hematological malignancies localized within the spine. The guideline is applicable in daily practice and provides an up-to-date and concise overview of the diagnostic and treatment possibilities for patients suffering from a disease that can have a serious impact on their quality of life. Suggestions for the practical implementation of patient care in hospitals are also provided, including approaches for pursuing proactive management. The crucial role of the patient in decision making is emphasized in this guideline.

Introduction

Global incidence rates of cancer are rising, mainly due to the ageing population [1,2]. These changes will translate to a predicted 20 million

new cancer cases worldwide by 2030, compared with an estimated 12.7 million cases in 2008 [3,4]. This increased incidence, combined with the longer survival of patients with cancer, has resulted in more people being confronted with metastatic disease, in which the skeleton is often

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affected [5–8]. Bone metastases most frequently occur in the spinal column [9]; postmortem examinations have demonstrated that spinal metastases are present in approximately 70% of patients with cancer [10]. More than 50% of spinal metastases are secondary tumors from breast, lung, or prostate carcinomas [11]. Multiple myeloma and sometimes lymphomas may also affect the spinal column [12,13].

Spinal metastases and spinal localizations may lead to back pain, spinal instability, pathological fractures and deformity. Furthermore, epidural growth or vertebral collapse may cause radiating neuropathic pain and neurological deficits because of the compression of the spinal cord or nerve roots, which severely affect the patient's quality of life. Consequently, the provision of information for patients, timely diagnosis, optimized local and/or systemic treatment, and adequate follow-up are of the utmost importance in the prevention or reduction of the progression of spinal metastases towards irreversible neurological damage.

In current clinical practice, the care management of patients with cancer and metastatic disease, including spinal metastases, is often reactive, responding to clinical symptoms rather than trying to proactively prevent complications. The optimal diagnosis and management of patients with spinal metastases requires a multidisciplinary approach. Although difficult to arrange, this is particularly important in emergency situations such as metastatic epidural spinal cord compression (MESCC).

The Dutch health system is a strong proponent of developing guidelines to reduce the nationwide variability in the treatment of many diseases. Many guidelines have been developed since the late 1990s, and are revised every five years [14,15]. These guidelines provide evidence- and consensus-based recommendations and requirements for the standard of care at a national level. Guidelines are also being developed internationally; for example, the American Society for Radiation Oncology (ASTRO), the Italian Orthopaedic Society (SIOT), and the United Kingdom's National Institute for Health and Care Excellence (NICE) have developed guidelines regarding the treatment/management of patients with (spinal) bone metastases [16–19].

In 2013, a national working group started to develop a new guideline for the treatment of patients with cancer and spinal metastases and patients with hematological malignancies localized within the spine. Four important principles were defined at the start:

1. The patient's perspective should lead the discussion. Patients themselves should have an important role in the decision-making process (patient participation).
2. Proactive management should be pursued, resulting in a rapid and adequate diagnosis and treatment and, as much as possible, the prevention of (the progression of) pain and the occurrence of neurological deficits.
3. Clear selection criteria for various treatments should be defined, taking into account the patient's spinal instability, spinal deformity, neurological prognosis, and life expectancy.
4. The organization, communication, and coordination of care should be optimized.

This paper describes the main results used in the evidence-based approach for the development of the Dutch national guideline on metastases and hematological malignancies localized within the spine. In addition, suggestions for its implementation are discussed, and practical considerations are provided to enable institutes to pursue the proactive management and organization of care.

Methods

In 2013, the Dutch Neuro-Oncology Working Group (LWNO), supported by the Netherlands Comprehensive Cancer Organisation (IKNL), formed a multidisciplinary expert working group tasked with drafting a guideline on spinal metastases. Since the symptoms, complications, and

treatments of hematological malignancies in the spine are very similar to those of spinal metastases arising from solid tumors, both are included in this guideline. Here, the term 'spinal metastases' includes spinal localizations of hematologic and solid-tumor malignancies, both with and without MESCC, unless otherwise specified.

The members of the working group represented all regions of the Netherlands, both university and general hospitals, and all relevant medical disciplines. All working group members were representatives of their national scientific associations, and had a mandate for their input. The working group members had expertise in anesthesiology/pain medicine, epidemiology, general practice, guideline methodology, hematology, medical oncology, neurology, neurosurgery, nursing, orthopedics, radiology, radiotherapy, and rehabilitation. Most importantly, a patient representative took an active seat in the working group to provide the patient perspective, and was considered a full member of the group. In total, the working group comprised 16 members. The organizing committee asked the federation of patients for their participation, which decided to be represented by one person.

A survey was performed amongst both healthcare professionals and patients to provide an inventory of the perceived bottlenecks in the various trajectories of patient care. The aim of this 'bottleneck analysis' was to provide an overview of all problems or challenges in clinical practice and, as a consequence, to determine the questions relevant for clinical practice. The bottleneck analysis was performed following the methods for developing guidelines outlined by the Dutch health system [20,21]. A list of these bottlenecks was sent out to all related scientific and medical associations and patient organizations in The Netherlands, asking them to (1) indicate whether they agreed with the identified bottlenecks; (2) prioritize the bottlenecks; and (3) indicate whether they perceived additional bottlenecks. In addition to the bottleneck inventory, six patients were recruited through the survey and were interviewed by telephone to gain insights into their perspectives. A total of 67 individuals responded to the bottleneck analysis, resulting in the identification of 17 bottlenecks in addition to the 15 that were initially defined. Subsequently, based on the importance assigned to the bottlenecks by the survey respondents and during discussions within the working group, 14 clinical questions were formulated (Table 1). These questions were addressed by the working group.

Three clinical questions were addressed using an evidence-based approach (questions 2, 4, and 5; Table 1). To answer these questions, a systematic literature search was performed and/or supervised by a literature researcher/methodology expert. In addition, the methodological quality (level of evidence) of the studies was assessed, enabling the assignment of a level of evidence to the guideline's conclusions and recommendations. The work was carried out in accordance with the Guideline for Guidelines [21]. Question 2 was addressed in accordance with the Evidence-Based Guideline Development (EBRO) approach, in which a level of evidence is assigned to each study [22]. The intervention questions (questions 4 and 5) were assessed in accordance with the Grading of Recommendations Assessment, Development and Evaluation (GRADE), in which a pre-defined level of evidence is assigned to each outcome measure [23]. Consequently, within a single study, one outcome measure can be categorized as being of high quality, while another can be assessed as being of low quality. The remaining 11 questions were answered using a consensus-based approach, which in practice meant that the literature search for these questions was carried out by the members of the working group themselves.

Each question was allocated to one of the working group members, based on his or her expertise, who acted as the chair for this issue. In subgroups of two to four group members, the search strategies and subsequently retrieved literature were discussed extensively. The analysis and writing processes for each question were also performed by the respective subgroup, after which the entire working group discussed and revised each chapter in plenary meetings. In total, eight plenary meetings corresponding to approximately 18 h of meeting time were held to discuss and revise the chapters.

Table 1
Clinical questions formulated based on the results of the bottleneck analysis.

Clinical question	Consensus- (CB) or evidence- based (EB)
1 What criteria must a patient with spinal metastases meet to be eligible for surgery followed by radiotherapy, or radiotherapy alone?	CB
2 Which factors should be used to most accurately predict the survival of patients with spinal metastases who are eligible for surgery and/or irradiation?	EB - EBRO ^a
3 How can the stability of metastatically affected vertebrae be determined in patients with spinal metastases, in view of a possible stabilizing operation?	CB
4 Which technique (simple versus advanced technology) and radiotherapy dose leads to the best possible outcome for patients with spinal metastases in terms of pain relief, mobility, morbidity, mortality, and cost?	EB – GRADE ^b
5 a. Does surgery via an anterior approach or surgery via a posterior approach offer a better outcome in terms of mobility, morbidity, mortality, complications, and progression-free survival in patients with symptomatic spinal metastases? b. Does surgery by means of an en bloc resection of the affected vertebra offer a better outcome than removing the vertebra by the piecemeal method or a partial resection (debulking), in terms of mobility, morbidity, mortality, complications, and progression-free survival in patients with symptomatic spinal metastases?	EB - GRADE
6 What is the effect of chemotherapy or hormonal therapy on the neurological deficit, pain, and quality of life in patients with spinal metastases?	CB
7 Which patients with spinal metastases are eligible for percutaneous interventions, such as radiofrequency ablation (RFA) and vertebroplasty, with a view to reducing symptoms (e.g. pain), in terms of morbidity, complications and mortality?	CB
8 Does the care trajectory in patients with spinal metastases require the involvement of a pain team?	CB
9 How can questionnaires (pain score, neurological functional scales) be used systematically in patients with spinal metastases?	CB
10 How is the need for psychosocial assistance detected in patients with spinal metastases and how is this assistance offered?	CB
11 Is multidisciplinary consultation always necessary for patients with symptomatic spinal metastases and how is this organized?	CB
12 Who follows up on the patient (and how)?	CB
13 How is an appropriate rehabilitation process established for patients with spinal metastases?	CB
14 Does the aftercare trajectory for patients with spinal metastases require the involvement of a rehabilitation specialist?	CB

^a EBRO: Evidence-Based Guideline Development.

^b GRADE: Grading of Recommendations Assessment, Development and Evaluation.

The patient advocate attended all working group meetings, actively participated in the discussions, and optimized the formulation of the patient's perspective in the draft texts. In addition, the working group verified whether the issues reported by the patients were sufficiently addressed in the guideline's conclusions and recommendations.

After approval from all working group members, the draft guideline was presented to the LWNO. The feedback from the LWNO members was in turn processed by the working group. The adapted draft guideline was then presented for comments to all scientific and professional associations and patient organizations that had been contacted within the framework of the bottleneck analysis, as well as to national and regional tumor working groups and the National Federation of Cancer Patient Organizations, resulting in the receipt of 145 comments from 25 respondents. The comments were evaluated and processed by the guideline working group. Eventually, the guideline was submitted to the relevant associations/authorities for authorization or approval, and the final guideline was published online in August 2015.

With the help of the patient advocate and a 'www.kanker.nl' editor, the information for patients was written and annexed into the guideline. This information is also available at www.kanker.nl [24], a national website that provides information to patients with cancer.

This paper describes the key outcomes of the guideline. The complete guideline has been translated into English and is freely available at www.oncoline.nl/spinal-metastases.

Results

This chapter describes the main findings of the guideline based on the four principles mentioned above.

The patient perspective

During the bottleneck analysis, patients identified the following points for improvement: having a say in their treatment, the lack of information on spinal metastases available to patients, the lack of psychosocial care, the value of multidisciplinary consultations, and delays in the exploration of symptoms that might indicate the presence of spinal metastases (doctors' delay). Extensive patient information on

spinal metastases has now been developed and is annexed to the guideline (Appendix A).

Proactive care management

Preventing unnecessary delay

A randomized trial demonstrated that 3% of 342 patients with painful radiated spinal metastases eventually show signs of MESCC [25]. Although the risk of developing neurological deficits is relatively low, the consequences can be debilitating. Most patients who are still ambulant at the time of diagnosis retain their ambulatory status if treatment is started in a timely manner [26]; however, if treatment is delayed until a patient is already bedridden due to severe neurological deficits, the chance of this patient regaining their walking ability is small [26,27]. To prevent progression towards a (complete) spinal cord injury or cauda equina syndrome as a result of symptomatic MESCC, it is therefore important to diagnose the patient as early as possible.

Considerable patient and doctor delays are unfortunately not uncommon [27,28], and are an important factor in the development of neurological deficits and other adverse outcomes that might be prevented by a faster course of action [26,29]. An important goal of the guideline is therefore to reduce delays caused by either patients or physicians.

Raising awareness about the symptoms

The guideline describes the symptoms that indicate the presence of spinal metastases, spinal instability, or myelum or cauda compression. These so-called 'alarm symptoms' are described in Table 2. The working group considered it vital that patients with bone metastases and their general practitioners (GPs) are properly informed about the likelihood of spinal metastases, the alarm symptoms that (urgently) require assessment, and who to contact in such cases. To this end, the working group developed a patient information sheet about spinal metastases, including the alarm symptoms and local contact information, which can be handed out to high-risk patients and their GPs (Appendix B). Of course, a broad range of healthcare professionals are confronted with patients with spinal metastases. To facilitate optimal collaboration and

Table 2

Alarm symptoms that indicate the presence of spinal metastases, spinal instability, and/or myelum or cauda compression.

Symptoms indicating the presence of spinal metastases in patients with cancer	Symptoms indicating spinal instability and/or myelum or cauda compression
<ul style="list-style-type: none"> – New and/or increasing severe back or neck pain – Pain between or just below the shoulder blades – Back pain when lying down (during sleep) that disappears when sitting up – Radiating pain in the stomach, chest, arms or legs 	<ul style="list-style-type: none"> – Decreased strength in the legs (and sometimes the arms) – Difficulty controlling the legs (and sometimes the arms) – A very wobbly gait – Numbness or tingling radiating down from chest, stomach, groin, and/or legs – Inability to walk and/or stand, or legs giving way

prevent delays, these healthcare professionals should all be informed about the guideline and the accompanying patient sheet outlining the alarm symptoms.

Clear deadlines for diagnosis and treatment

In addition to delays caused by patients, doctors can also delay the diagnosis and treatment of spinal metastases. The guideline contains recommendations and sets clear deadlines for imaging studies when spinal metastases are suspected (Fig. 1). Spinal metastases cannot be excluded using conventional x-rays, CT scans, or bone scintigraphy [28,30]; therefore, full spinal column Magnetic Resonance Imaging (MRI) is the first choice for diagnosing patients when there is a clinical suspicion of spinal metastases. MRI is superior to all other imaging modalities when it comes to demonstrating spinal metastases and the compression of the myelum or cauda [31–36]. Both T1- and T2-weighted images are required to demonstrate spinal metastases and, in particular, spinal epidural metastases and/or MESSC [31,37,38]. The deadline for MRI scanning depends on the nature of the patient's complaints (Table 3); an MRI should be performed within two weeks when the patient has only local back pain, or within 12 h if there is a clinical suspicion of MESSC, to enable treatment to start promptly.

In patients with suspected spinal metastases of an unknown origin, there is a need to urgently obtain a histological diagnosis before the treatment can start. The diagnostic timeframe in these patients depends on their (risk of) neurological deficits (see Fig. 1).

Treatment selection

The guideline extensively addresses a broad range of treatment modalities for patients with spinal metastases with respect to their effectiveness on pain and neurological problems, including radiotherapy, surgery, systemic treatments, and percutaneous interventions. Based on the available literature, the working group developed a flow diagram describing the recommended selection of treatments based on the patient's estimated survival, estimated spinal (in)stability, and expected treatment outcome (Fig. 2).

In general, radiotherapy is the first choice of treatment in patients with symptomatic spinal metastases (with pain and/or neurological deficit), provided that an adequate radiotherapy dose can be given. To be eligible for surgery, the patient must have a life expectancy of at least three months, a good clinical situation, and a limited area of damage and/or obstruction. Surgery is the preferred treatment in case of (1) spinal instability; (2) the recurrence or progression of pain and/or neurological deficits following radiotherapy or where repeat radiotherapy is not possible; and/or (3) neurological deterioration under radiotherapy and corticosteroids. For the treatment of MESSC-induced neurological deficits, surgery and radiotherapy are equivalent options. The choice of treatment should be made on the basis of a (ad hoc) multidisciplinary discussion (see 4.1), and should incorporate patient preference following the concept of shared decision making. Detailed information on the types and dosages of radiotherapy and the types of surgery are described in the guideline.

Systemic treatment is provided as a primary treatment if there is a high chance of response (e.g. in multiple myeloma and some types of malignant lymphoma).

Assessing survival

An accurate assessment of life expectancy is required to prevent both overtreatment (extensive surgery in patients with a short-term survival expectancy) and undertreatment (forgoing treatment in patients with prolonged survival); however, two systematic reviews showed that the assessment of life expectancy by physicians based solely on their clinical experience is inaccurate [39,40].

The literature describes several prognostic models that can be used as a tool for predicting survival using patient-specific risk factors. Four externally validated models including at least the risk factors primary tumor and performance status were identified: the Tokuhashi [41], Van der Linden [25], Bartels [42], and Bollen [11] models. Details of these prognostic models can be found in Table 4. The accuracy of the Tokuhashi model is reported to vary greatly [43–47], but the other models have been shown to permit a reliable assessment of the survival of patients with symptomatic spinal metastases, with no model being superior to the others [11,48,49].

Assessing spinal (in)stability

The Spinal Instability Neoplastic Score (SINS) is the first attempt to register mechanical instability due to metastatic disease [50]. The SINS was developed to help physicians gain insight into the degree of spinal instability using six radiological and clinical components. Although the SINS is reproducible and has good inter- and intra-observer agreement [51,52], to date no prospective study has been published validating the SINS's predictive power to differentiate between spinal lesions at risk of progressive debilitating instability. The use of SINS as an absolute tool to differentiate between stable and unstable spines when making the decision whether or not to perform surgery is not advised in this guideline. For now, spinal (in)stability is judged clinically and radiologically. It is recommended that all cases involving patients with a (potentially) unstable spinal column are discussed with a spinal surgeon.

Organization of care

Multidisciplinary cooperation

Determining the best treatment for a patient with spinal metastases is a complex process that requires a multidisciplinary approach. Multidisciplinary consultation (MC) meetings are mentioned increasingly often in guidelines and indicator sets [15,53,54]. Fitzpatrick et al. [53] demonstrated that the number of incorrect referrals of patients for epidural spinal metastasis surgery is reduced when a prior virtual consultation (by email, telephone, and imaging via the online PACS system) with the spinal surgeon takes place. Although there is no other evidence to support the effectiveness of an MC meeting for patients with spinal metastases, the guideline committee believes such meetings are essential for the optimal proactive management of patients with spinal metastases. All patients with symptomatic spinal metastases should be discussed in an MC meeting involving a representative of the original treating medical specialty (e.g., medical oncologist, hematologist), a radiation oncologist, a radiologist, a neurologist or neuro-oncologist (in case of neurological deficits), and (in cases with a potential

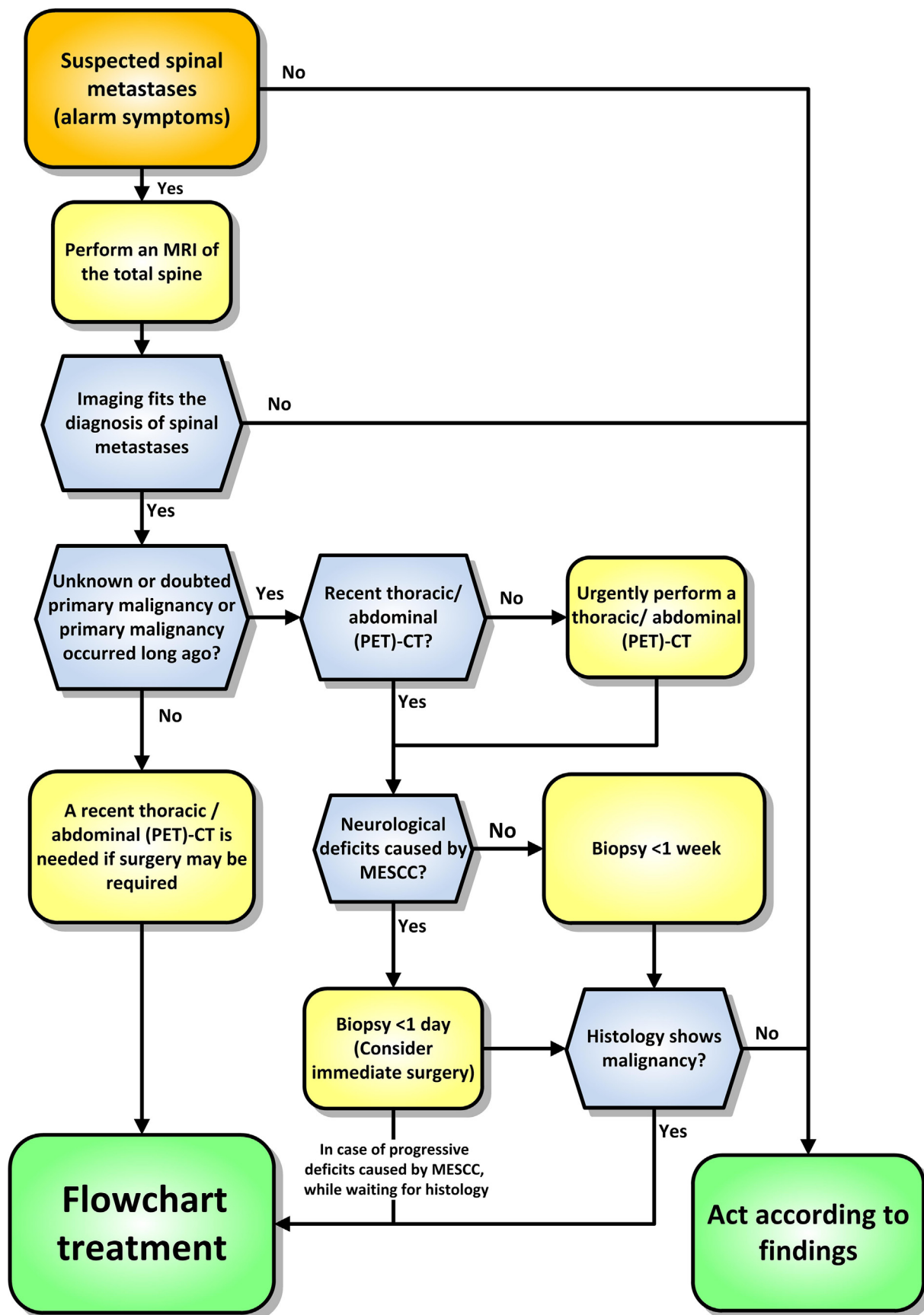


Fig. 1. Flowchart on diagnostics in patients with suspected spinal metastases or spinal localization of hematological malignancies. CT: Computed Tomography; MESCC: Metastatic Epidural Spinal Cord Compression; MRI: Magnetic Resonance Imaging; PET: Positron Emission Tomography.

Table 3
Indications and deadlines for MRI scanning.

Symptom	Deadline for MRI scanning
Only local back pain	Within two weeks
Unilateral radicular pain	Within one week
Unilateral radicular deficit that develops over more than seven days and has a progressive nature	Within 48 h
Unilateral radicular deficit that develops within seven days and has a progressive nature	Within 24 h
Clinical suspicion of MESCC ^a	As soon as possible, but at least within 12 h

^a In the case of MESCC, treatment should start well within 24 h after MESCC is diagnosed.

need for surgery) a spinal surgeon. This consultation can take place during a weekly structured MC meeting, but in urgent cases such as a patient with a progressive neurological deficit, an ad hoc consultation with at least the responsible physician, a radiation oncologist, and a spinal surgeon is required.

Optimal palliative care

With the exception of malignancies that can be cured using chemotherapy (e.g. non-Hodgkin lymphomas), most patients with spinal metastases are in the palliative phase of their disease. According to the World Health Organization, palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness through the prevention and relief of suffering, by means of the early identification and impeccable assessment and treatment of pain and other physical, psychosocial, and spiritual problems [55]. Such care involves a substantial change in the way patients and their relatives are approached. The current palliative care guideline emphasizes that attention should be paid to all aspects of care: physical, psychological, social, and spiritual [56].

In addition, the potential for appropriate actions to be taken to achieve optimal functionality should be investigated, taking into account the patient's wishes and life expectancy. The possibilities to (re) gain function by means of, for example, a rehabilitation program, physical therapy, or occupational therapy should therefore be explored.

Coordination of care and communication

The coordination of care and the optimal communication between all healthcare professionals is essential for the best possible care for patients with spinal metastases. It is therefore vital to designate the responsible physician, i.e. the clinician who is the first point of contact for the patient and other care providers, who also controls and coordinates the care provided to the patient. In the disease oriented phase of care, this will often be a medical specialist in the hospital, such as a medical oncologist or hematologist. During symptom-oriented phase of care, the responsibility increasingly shifts to the GP or geriatric specialist. The principal care provider will ensure a proper, preferably verbal and written, transfer of care for this transition of responsibility, which may involve a transfer within the hospital or a transfer from the hospital specialist to a GP. Patients should be well aware of who their responsible physician is at all times.

Ideally, the patient's GP should play a central role, and therefore be actively involved in the care trajectory as early as possible. Ensuring the GP is well-informed of the situation at all times is therefore desirable, including the knowledge of which vertebrae are affected (the results of most recent diagnostic imaging), what symptoms can be expected, what to do in case of such symptoms, and the possible options for treatment. In complex situations, a palliative care team should be available for consultation by the GP or specialist at all times.

Discussion

The Dutch national guideline on spinal metastases from solid tumors and hematological malignancies not only focuses on treatment choices, but also addresses important topics such as proactive care to prevent of complications, proper patient categorization using predictive models, multidisciplinary collaboration, and the optimal organization of care, all based on the needs and wishes of the patient.

Discrepancies often exist between the best clinical practices determined by scientific evidence and the actual care provided to patients; about 30–40% of patients do not receive care based on the current scientific evidence, and about 20–25% of the care provided is unnecessary or even potentially harmful to patients [57]. Clinical guidelines aim to standardize and improve patient care by providing recommendations for appropriate and optimal care in specific clinical circumstances, based on an integration of clinical expertise, the best evidence available, and patient wishes. Understanding the factors that facilitate or hinder changes in clinical practice can allow implementation strategies to be tailored for use, and could help to bridge the gap between scientific evidence and patient care [58]. Therefore, below some additional comments are made on the issues raised in the guideline.

The proactive management of care is targeted by reducing the delays in the diagnosis and treatment of spinal metastases caused by both doctors and patients. The guideline emphasizes that this delay can be handled on two levels, both by increasing patient and doctor awareness of the alarm symptoms indicating the presence and complications of spinal metastases and by setting clear deadlines for the appropriate and timely diagnosis and treatment of spinal metastases. This aids in preventing – as much as possible – debilitating clinical symptoms such as progressive pain, spinal instability, and/or neurological deficits.

In the guideline, we emphasize a proactive treatment of epidural metastases; however, the initiation of every treatment occurs after a patient complains of one or more symptoms. Ideally, treatment would begin just before such complaints occur, but we are not currently aware of a modality to predict who will suffer from symptomatic metastases. Screening everyone with a malignant cancer diagnosis for spinal epidural metastasis will not contribute to an increased quality of life and is certainly not cost-effective. The possibility of predicting spinal metastases could be a very interesting topic on which to focus future research.

The education of patients and clinicians, both hospital specialists and GPs, should focus on recognizing the alarm symptoms. We have published parts of the results of the Dutch guideline in a Dutch general medical journal that targets a broad audience, thereby educating clinicians and raising awareness about the alarm symptoms and the existence of the new Dutch guideline [59,60].

Distributing information on the presence and complications of spinal metastases is challenging, as patients with cancer are seen by and treated in numerous institutes and by various clinicians, including GPs. It therefore requires inter-institution and interdisciplinary communication between clinicians, with clear agreements on who furnishes the patient with information including the alarm symptoms. These working arrangements, together with the patient information sheet, should be easily accessible through a content management system. Moreover, adopting information about the alarm symptoms on websites for patients with cancer and supplying the information in patient information brochures for each of the involved medical specialties might enhance the education of patients. To this end, the information for patients has been made available online on a national website designed for patients with cancer (www.kanker.nl), as well as on a website comprising a database of oncology-related guidelines [15]. Finally, a responsible physician should be accountable for ensuring that patients are adequately informed.

Easy access to diagnostic imaging and treatment, i.e. radiotherapy and spinal surgery facilities, should be available to enable timely diagnosis and treatment. The guideline sets clear and relatively tight

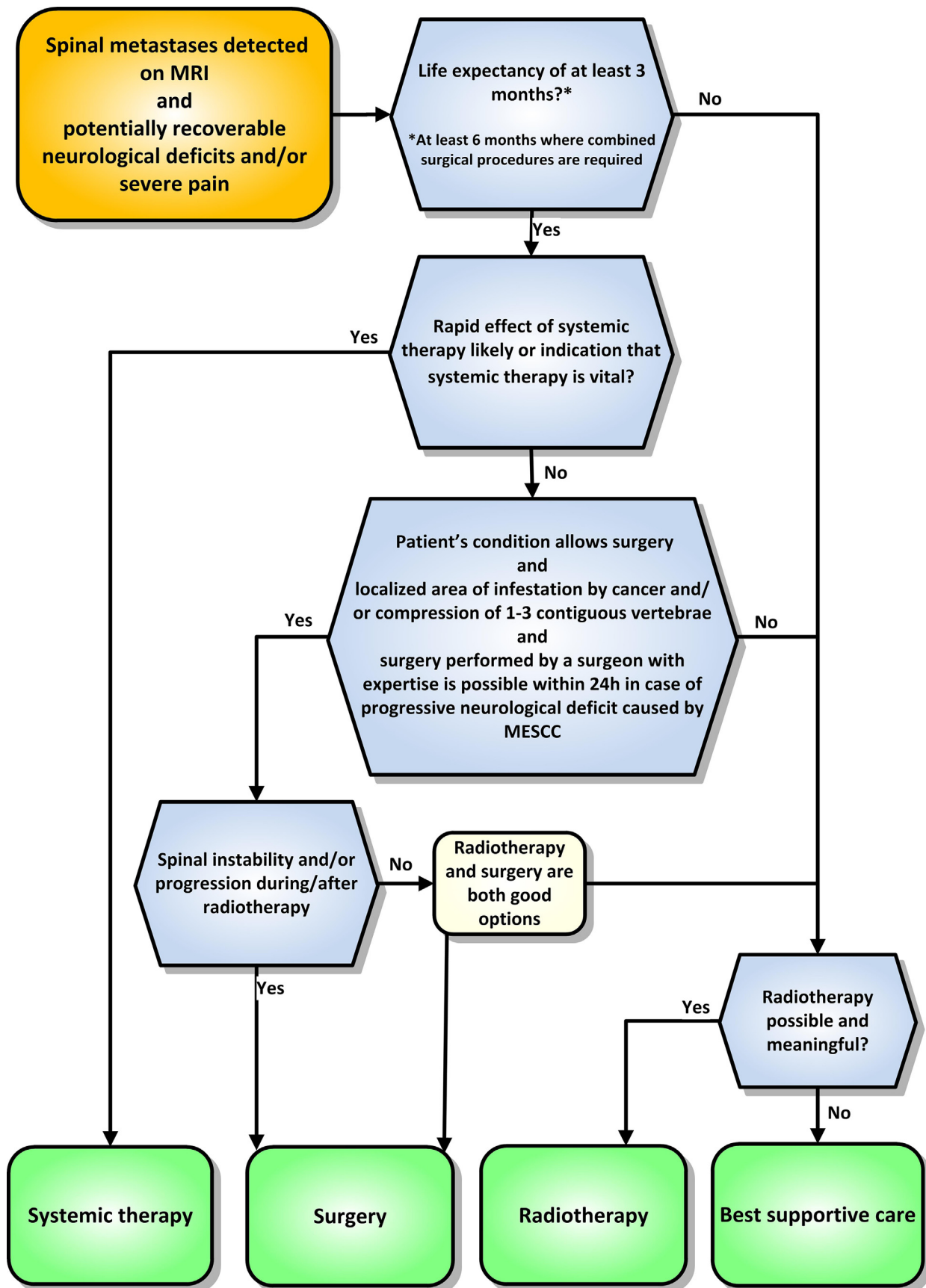


Fig. 2. Flowchart on treatment selection in patients with symptomatic spinal metastases. MESCC: Metastatic Epidural Spinal Cord Compression. MESCC: Metastatic Epidural Spinal Cord Compression; MRI: Magnetic Resonance Imaging.

Table 4
Details of prognostic models on survival.

	Tokuhashi	Van der Linden	Bartels	Bollen
Original population (n=)	246	342	219	1043
C score ^a	0.640	0.664	0.719	0.710
Risk factors incorporated in the model				
– Primary tumor	X	X	X	X
– Performance status	X	X	X	X
– Visceral metastases	X	X		X
– Bone metastases	X			
– Number of spinal metastases	X			
– Neurological functioning	X			
– Location of spinal metastases			X	
– Gender			X	
– Curative tumor treatment			X	

^a The C score contains an estimation of the probability of similarity between the predicted and observed survival rates. The C score may vary from 0.50 (no predictive value) to 1.0 (complete similarity between predicted and actual survival).

deadlines for diagnostics, depending on the severity of the patient's symptoms, and it is important that institutions maintain a policy that allows rapid access to diagnostic imaging.

The treatment selection criteria provided in the guideline are based on the patient's estimated survival, degree of spinal instability, and expected treatment outcome. To estimate survival, the prognostic models published by Van der Linden et al. [25], Bartels et al. [42], or Bollen et al. [11] are recommended in the guideline. It must be noted that, although these models show comparable results, the populations of patients with spinal metastases on which the models are based vary greatly; for instance, the Van der Linden model contains patients with only pain as a symptom, while about 50% of the Bollen patients had neurological symptoms, and in the Bartels population, 84% of patients had neurological complaints. These models have been developed and partially validated in Dutch patients and are therefore considered to be valid for use with Dutch patient populations. The Van der Linden model has already been successfully validated in the Canadian population [49] and the Bartels model has also been geographically and prospectively validated [48,61]; nevertheless, these models should be validated further for truly international use. These models were based on current clinical practice; however, new treatment options are currently being developed, and are expected to increase the survival of patients with spinal metastases. New insights have recently been provided into the effects of tumor profiles and mutation status on patient survival [62,63]; thus, existing prognostic models should be continuously updated.

Although additional literature concerning the SINS has become available since the publication of the guideline [64–67], the prospective validation of the SINS's predictive power to discriminate between spinal lesions at risk of progressive debilitating instability is still lacking. In addition, more recent studies have reported contradictory findings on the inter- and intra-rater reliability of the SINS [52,66,68,69]; therefore, the guideline advises against the use of the SINS as a predictor for progressive spinal instability. It could, however, be useful as a tool for streamlining the communication between physicians of different medical specialties and for facilitating decision making during surgical consultations.

With regard to the organization of care, the guideline recommends discussing all patients with symptomatic spinal metastases in a multidisciplinary meeting. Weekly MC meetings already take place in several hospitals, both academic and otherwise. For more acute situations such as cases involving MESCC, severe pain, and/or spinal instability, treatment must be initiated quickly, and there is usually no time to wait for the weekly multidisciplinary meeting. In such cases, an ad hoc

consultation should be arranged, ideally in person, but a meeting over the telephone or using more modern technologies such as Skype and the digital transfer of PACS images offer additional solutions. These technologies may also be of benefit if the physicians are working in different institutions or at different locations.

In addition, the guideline advises that the physician responsible for a patient's care should be clearly identified to both the patient and all other caregivers, as well as being registered in the patient's file. It is also recommended that the responsible physician's tasks and responsibilities are formalized.

Ongoing initiatives are creating regional cancer networks of all stakeholders, from GPs to tertiary referral centers (e.g., for spinal surgery or radiotherapy). Within these networks, agreements on the organization, monitoring, and continuous improvement of care are being made, ensuring that all patients in their respective geographic regions benefit from the best-quality care available. In the Netherlands for example, regional Comprehensive Cancer Networks are being established, while the NICE guideline describes the formation of cancer networks within the United Kingdom.

The current guideline prescribes a prominent role for the GP in the care of patients with spinal metastases. In the Netherlands, all citizens are registered with a GP (also termed a family doctor or family physician) who offers primary care, which is reimbursed by the patient's (mandatory) health insurance. As a result of this easily accessible primary care, Dutch GPs have a good overview of the health status of their patients, can play a major role in their palliative care, and may serve as the responsible physician; however, we acknowledge that the role of the GP may be different in other countries.

Conclusion

This national multidisciplinary guideline aims to improve the quality of care for patients with cancer and spinal metastases and hematological malignancies and, consequently, improve their quality of life. Four important principles are defined: (1) the patient's perspective leads the discussion; (2) proactive management is directed at preventing complications; (3) clear treatment selection criteria are defined; and (4) the organization, communication, and coordination of care is optimized. The guideline explicitly pursues proactive, multidisciplinary patient care and gives recommendations about diagnostics, treatment modalities, patient selection, follow-up, organization of care, and palliative care. Finally, practical considerations regarding the implementation of the guideline are also discussed.

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Conflict of interest

None.

Author contributions

All authors made substantial contributions to all of the following: (1) the conception and design of the study, the acquisition of data, or the analysis and interpretation of data; (2) drafting the article or critically revising it for important intellectual content; and (3) approved the final version of this manuscript.

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Appendix A. Supplementary material

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