Perioperative Safety in Middle-Income Countries

Jose Andres Calvache España

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Perioperatieve veiligheid in landen met een gemiddeld inkomen

Thesis

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TABLE OF CONTENTS

SECTION 1

INTRODUCTION AND OUTLINE OF THE THESIS

INTRODUCTION AND OUTLINE OF THE THESIS

To understand the subjects presented in this thesis, this introduction will address general issues on quality and safety with a focus on perioperative settings, some broad ideas about patient safety and safety culture and lastly, some topics about interventions to improve patient safety with a particular focus on middle-income countries.

Quality, safety and patient safety

Safety is the state of being "safe", a condition of being protected from harm or other non-desirable outcomes (despite permanent threatening). Safety can also refer to a "steady state" of an organization or place doing what it is supposed to do appropriately or to the control of recognized hazards in order to achieve an acceptable level of risk (1). Even with continuous alertness, health care providers face many challenges in today's environment in trying to keep patients safe with particular importance during the perioperative period (2).

The Institute of Medicine defines "quality in health care" as the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge (3,4). Currently, many authors and organizations consider patient safety indistinguishable from the delivery of quality health care.

Patient safety incorporates a complex continuous process including awareness about quality and safety, prevention of harm, assessment of patient safety, reporting of incidents, damage control, incident analysis, process of improvement and finally, improvement. Patient safety has emerged as an important part of a system of care delivery that prevents errors, learns from the errors that do occur and is built on a culture of safety that involves organizations, hospitals, health care professionals and patients (3,4).

Any human system, anesthesia, surgery and health care in general, have inherent risks and those risks can vary among populations, including between and within countries, specific settings and individual providers. In order to minimize those risks, studying patient safety can provide feedback to healthcare systems with the possibility of implementing improvement measures based on the identification of specific problems at different areas (2,5).

Perioperative mortality has declined significantly over the past 50 years, with the greatest decline in developed high-income countries (6). Lienhart et al, estimated a 10-fold decrease in anesthesia-related mortality in 1999 compared to 1982 (7). Bartels et al, stated in 2014 that the magnitude of all-cause perioperative mortality (including perioperative myocardial injury) approximated the third leading cause of death in the United States, just after heart diseases and malignant neoplasm (8). These findings must be interpreted taking into account the increasing patient baseline risk, age, comorbidi-

ties and complexities of modern perioperative care. The surgical mortality in developing countries is 10 times higher than in developed nations (9) and deaths attributed only to anesthesia could be as 1000-fold higher (10–12). Even in patients with a low-risk profile, Biccard et al, showed how patients in Africa were twice as likely to die after surgery when compared with the global average for postoperative mortality (13).

In 2015, the Lancet Commission on Global Surgery launched the Global Surgery 2030 strategy, an effort to discuss the important role of perioperative care as a major public health concern. It aims to improve the development of anesthesia and surgery in developing countries with the close support of actors from high-income countries in order to build the surgical systems of the future (14,15). One of the key messages of this consensus is that currently, 5 billion people lack access to safe, affordable surgical and anesthesia care when needed worldwide (15).

Several aspects of patient quality and safety deserve attention in low- and middle-income countries. A study involving all patients in 58 hospitals from five Latin American countries reported an estimated prevalence of adverse events in health care of 10.5%. Six percent of these events were associated with the patient's death and more than 28% caused disability. Almost 60% of the total group of adverse events was judged to be avoidable (16). In that sense, encouraging patient safety as a cornerstone of a high-quality health care system should be a priority in perioperative management.

Since 1993, the Colombian healthcare system is known as "Sistema General de Seguridad Social en Salud (The General System of Social Security in Health)". This is an obligatory national health insurance system where formally employed individuals, retirees or self-employed individuals earning at least the minimum wage must contribute to the system through a mandatory payroll deduction (contributive regime) and individuals from the low-income population (near 23 million) are affiliated through governmental subsidies (subsidized regime) (17,18). At the end, definite providers of care have been divided into public and private hospitals with a broad ranges of quality. This is an indicator of raging inequities within Colombia's health care system, which has been lauded for providing near-universal coverage (most than 95% of the population) but widely criticized for providing dramatically inferior care to the population with less resources. As a consequence, patients with private insurance enjoy better chronic disease outcomes and lower infant and maternal mortality rates than those with government-subsidized insurance (19–25).

Colombia is a predominantly urban country (76% of the population) of over 48 million inhabitants (18). There is a widespread variability in the system across the country. Urban settings show top-quality hospitals and educational programs while rural remote locations have a deficient, fragmented and disorganized healthcare system. Additional and important barriers to provide a high-quality and safe perioperative care include big scandals of bureaucracy and corruption in the management of the system and a grow-

ing poor understanding of the healthcare as a business (26). This diversity represents a strong challenge for patient safety making any intended measure or intervention would be adapted depending on the level of care pretending to improve. Considering this context, the general aim of this thesis was to explore areas of potential improvement of patient quality and safety in perioperative period whilst accounting for attainable research scenarios.

Safety culture

The concept of "safety culture" has its origin outside of the healthcare sector, in studies of high reliability organizations that consistently minimize adverse events despite carrying out inherently complex and hazardous work (such as petrochemical industry, nuclear industry and aviation). High reliability organizations maintain a commitment to safety at all levels, from frontline providers to managers and executives (27). Due to its inherent nature as a social construct, safety culture has been defined in a variety of ways in health care and other industries. Some see safety culture as patterns or behaviors of responses to problems while others define it more narrowly, focusing on the key dimensions of unit and organizational leadership's prioritization of safety (28–30). Patient safety is sometimes broadly conceptualized to include sub-dimensions such as learning, reporting, blame orientation, job satisfaction and staffing attitude (28,31–34).

However, to assess the patient safety "culture" directly is not easy. As a surrogate, the "climate of patient safety" can be measured and analyzed at different levels of the health care system including perioperative settings. It allows to identify strengths and weaknesses that configure the way that health care professionals approach their work and how they think and behave. Culture assessment tools help to understand the underlying mechanisms and provide the ingredients for an action plan to improve patient safety taking into account that in order to transform a culture, it is important to first measure and analyze it (2).

Assessment of the safety culture at perioperative period reminds the classical definition of the Hawthorne effect -also referred as observer effect- well-known in research in controlled scenarios (35,36). Hawthorne effect is a type of reactivity in which individuals modify certain characteristics of their behavior in response to their awareness of being observed or studied (36). A definition of patient safety -adjusted to culture-, should consider the question: what are we doing when nobody is watching?.

Interventions

By definition, "culture" is the system of shared beliefs, values, customs, behaviors, and artifacts that the members of society use to cope with their world and with one another, and that are transmitted from generation to generation through learning (37,38). Regional influences, beliefs, values and attitudes, in addition to economic and social

status, are in close relation with the "patient safety culture" at any level of health care. It explains why some interventions may have a reduced acceptance in certain populations (i.e. certain countries) despite its effectiveness in others (12,39,40).

Assessment of patient safety and some procedure-specific interventions should be topics of high interest in countries like Colombia. Unfortunately, improvement of perioperative care is addressed with low priority in low- and middle-income countries (15,41,42). Common techniques and practice of procedures like central venous catheterization are poorly investigated in Colombia despite their daily usage, as well as anesthetic care of obstetric patients during cesarean section or during evacuation of an incomplete miscarriage. These scenarios are part of this thesis.

Central venous catheterization is a very common procedure performed by anesthesiologists, surgeons and many related specialties not only during the perioperative period. Mechanical complications have an estimated incidence around 20% and current practice guidelines support the use of ultrasound guide in order to ensure safety during the positioning of the catheter (43,44). There is a lack of information from low- and middle-income countries in terms of perceptions about safety during the procedure, limitations for the use of ultrasound devices and determinants of mechanical complications.

An incomplete miscarriage occurs when all the products of conception are not expelled through the cervix, retaining tissues in the uterus. Traditionally, surgery (curettage or vacuum aspiration) has been the treatment used to remove any retained tissue and it is quick to perform. This thesis summarizes the potential anesthetic techniques to provide during this procedure and the available evidence.

Finally, a caesarean section can be a life-saving intervention when medically indicated. Given its increasing use, ensuring quality and safety includes avoiding frequently occurring adverse outcomes with potential health effects for women and children like maternal hypotension during anesthesia (45,46).

This thesis presents a broad spectrum of epidemiological designs and methods starting from observational studies (surveys, cross-sectional studies and cohort studies) until clinical trials and systematic reviews, all designed to evaluate areas of interest at local, regional and national level of Colombia. To some extent, these measures and interventions could be transferred and applied to other low- or middle-income countries.

OUTLINE OF THE THESIS

Based on the background described above, this thesis summarizes the research questions and possible answers based on the scientific work of the author over more than 10 years of Colombian-based research with direct support and supervision of Department of Anesthesiology of Erasmus Medical Center Rotterdam, The Netherlands.

The publications presented here are clustered around 3 key-questions:

Question 1: What is the current state of Randomized Controlled Trials and Systematic Reviews on Patient Safety worldwide?

Chapter 1 describes randomized controlled trials and systematic reviews on patient safety published from 1973 and 2010. From studied interventions and number of papers published on the topic to a broad overview of the safety-related literature, the most relevant issues are addressed in this review.

Question 2: Is there any validated approach to assess safety in perioperative care in middle-income countries like Colombia?

The research presented in chapter 2 examines the psychometric properties of the Latin American Colombian translation of the Hospital Survey on Patient Safety Culture questionnaire for use in perioperative setting and evaluates if its original version could be used. In addition, it provides an overview of the state of safety climate in a third-level of care hospital in Colombia and potential areas of improvement.

Question 3: Which perioperative interventions on quality and safety potentially affect patients in low- and middle-income countries?

Chapters 3 to 6 focus on important areas of quality and safety in low- and middle-income countries. First, the current practice of central venous access and potential use of technology to improve safety during catheterization in Colombia (chapters 3 and 4). Subsequently, chapter 5 summarize evidence on anesthetic techniques for a very common surgical procedure in low- and middle-income countries like the evacuation of an incomplete miscarriage and finally, in chapter 6 we tested whether the use a low-cost positioning intervention could improve quality and safety of spinal anesthesia for cesarean section.

In the final, general discussion chapter review the findings of the papers presented and address future perspectives.

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SECTION 2

GENERAL ASPECTS OF PERIOPERATIVE SAFETY

Chapter 1

Identification and Description of Randomized Controlled Trials and Systematic Reviews on Patient Safety Published in Medical Journals.

Barajas-Nava LA, Calvache JA, López-Alcalde J, Solà I, Bonfill-Cosp X.

J Patient Saf 2013;9(2):79-86.

ABSTRACT

Objective

To identify and describe randomized controlled trials (RCTs) and systematic reviews (SRs) on patient safety published from 1973 onward.

Materials and Methods

We handsearched a total of 12 medical journals published in English with contents related to patient safety to identify RCTs and SRs published between 1973 and the end of 2010. The results obtained from this search were complemented with an additional search in MEDLINE. The documents were classified by area of specialty or service in which the intervention was applied, level of preventive action, and type of patient safety incident, the latter in accordance with the International Classification for Patient Safety proposed by the World Health Organization (WHO). The main features of the identified studies are also described.

Results

A total of 787 issues of 12 journals published between 1973 and 2010 were handsearched. This procedure yielded 10,162 references, of which, 131 corresponded to RCTs and 127 to SRs. A parallel MEDLINE search identified only about two-thirds of these articles. Of all the studies identified, 83 RCTs and 64 SRs addressed interventions related to patient safety. The types of incident related to patient safety that were included most often in RCTs involved the clinical process, and for SRs, those related to resources/organizational management. On average, only 3.5 RCTs and 3.4 SRs were published per year, many of which had significant deficiencies in the reported information, such as, for instance, a lack of details on the methodology used.

Conclusions

The number of RCTs and SRs on patient safety published in specialized journals is scarce. No studies on interventions to improve the safety of the handling of blood and derivatives, infections related to health care, nutrition, or infrastructure were identified as a result of our search. Handsearching plays a key role in the identification of all the clinical trials that could be included in SRs on patient safety interventions. Knowing the content of RCTs and SRs published on patient safety can better target future research.

Keywords

patient safety, randomized controlled trials, systematic reviews, meta-analysis

PATIENT SAFETY

Patient safety is the reduction of risk of unnecessary harm associated with health care to an acceptable minimum. An acceptable minimum refers to the collective notions of given current knowledge, resources available, and the context in which care was delivered weighed against the risk of nontreatment or other treatment. Health care-associated harm is a significant source of morbidity and mortality worldwide. (1,2) Studies suggest that between 4% and 17% of hospitalized patients experience an adverse event (AE). (3-13)

An AE is defined as an untoward incident, injury, or unnecessary harm that is caused by health-care delivery rather than by the underlying disease process and that can result in complications, prolonged hospitalization, disability on discharge, or death. (1,2,6,7) Moreover, it is estimated that approximately 50% of the AEs are preventable. (3) Given the world-wide necessity to improve health-care safety, the World Health Organization (WHO) announced in 2004 the launch of the World Alliance for Patient Safety, (14) which aims to make health-care safety a top priority in the health agendas of all countries.

Research in patient safety plays a key role in improving the quality of health care. However, despite the effort invested in this field during the last 20 years, the more effective interventions to prevent or minimize the damage associated with AEs, and the most appropriate strategy to implement them, remain relatively unknown. To address this issue, the World Alliance for Patient Safety created a working group to identify priorities for research in patient safety, which took into consideration the frequency of adverse events, the severity of damage generated on the patient, and their impact on the health system. Thanks to this work, 50 topics were identified for research, including adverse events related to medications, injuries caused by health products, health care-associated infections, and injuries from falls in hospitals. (2,15,16).

Evidence on the Effects of Interventions to Improve Patient Safety

Research on patient safety is a relatively recent practice. Scientific output in this field has increased dramatically in recent years and, as a result, evidence on practices to improve patient safety is increasing. (17) However, research on the efficacy of the interventions to decrease unnecessary risks associated with health care presents peculiarities. For instance, they are often "complex interventions" that target on groups of subjects in an equally complex environment, such as health organizations. (18,19)

In general, the best available research design to evaluate the efficacy of health interventions is the randomized controlled trial (RCT), which is the study design that provides the most robust evidence. (20-24) The term controlled clinical trial (CCT) was incorporated into the electronic bibliographic databases during the 1990s; thus, CCTs that had been published previously were classified in other categories, hindering their identification. Additionally, in many cases, the study authors do not clearly describe

the methodology used, which makes the classification of their studies more difficult. Despite efforts to improve documents indexation in databases, the sensitivity of electronic searches remains unsatisfactory. (23-28) Hence, if the purpose of an electronic search is to comprehensively identify all published RCTs, as is the case when conducting a systematic review (SR), handsearching is an indispensable complement to obtain the best available evidence. (27,29,30)

In recent years, there have been numerous studies aimed to identify all RCTs published on various health topics, (31-37) but none has identified clinical trials and systematic reviews on patient safety. Therefore, we conducted this study to identify and describe RCTs and SRs that have been published in the most relevant journals on patient safety.

MATERIALS AND METHODS

We selected the 12 journals published in English that, in our opinion, addressed more specifically topics related to patient safety and the health-care quality. These journals were reviewed through handsearch for the period between 1973 and 2010 (Table 1).

One author (L.B.-N.) handsearched the previously chosen journals to identify RCTs and SRs published in each volume. This process consisted of a careful review of every article in each issue, including letters to the editor, abstracts, and conference presentations. Studies that met the following criteria were eligible for inclusion: RCTs (with assignment of subjects to each arm of the study using a random method, where the unit of randomization could be individuals, groups, or body parts) or SRs (without restrictions by study designs) that compared 2 or more interventions, of which, at least one was on patient safety. A patient safety intervention was defined as any intervention designed to reduce the unnecessary risk of harm associated with health care to an acceptable minimum. (2,18,38) With this in mind, any intervention that sought to prevent or detect patient safety incidents or mitigate their consequences was considered as eligible. A patient safety incident was defined following the criteria of the conceptual framework for the International Classification for Patient Safety (v 1.1): "an event or circumstance that could have resulted, or did result, in unnecessary harm to a patient. The use of the word 'unnecessary' in this definition recognizes that errors, violation, patient abuse and deliberately unsafe acts occur in healthcare.

These are considered incidents. Certain forms of harm, however, such as an incision for a laparotomy, are necessary. This is not considered an incident." According to this framework, a patient safety incident could be a reportable circumstance, near miss, no harm incident, or harmful incident (adverse event). (1) Interventions could be pharmacological, surgical, educational, organizational, or otherwise. When several reports that referred to the same RCT were found, only the original report was considered. In

Table 1. Handsearched Journals (1973-2010)

Journal	Review Period
Health Services Research	1973-2010
Journal of Safety Research	1982-2010
Quality and Safety in Health Care	1992-2010
Injury Control and Safety Promotion	1994-2005
The Joint Commission Journal on Quality Improvement	2000-2002
Joint Commission Journal on Quality and Safety	2003-2004
Joint Commission Journal on Quality and Patient Safety/Joint Commission Resources	2005-2010
Journal of Health Services Research & Policy	2001-2010
BMC Health Services Research	2001-2010
Quality Management in Health Care	2001-2007
International Journal of Injury Control and Safety Promotion	2005-2010
Journal of Patient Safety	2005-2010

addition, SRs with or without meta-analysis that evaluated the effects of an intervention on patient safety were eligible.

The search process consisted on an initial reading of the titles of the articles published in each issue. When this reading did not provide sufficient information regarding a particular article, keywords of its abstract were reviewed, such as randomization/randomized, quasi-random, controlled trial, blinding or masking, open clinical trial, prospective study, control group, placebo, systematic review, or meta-analysis. Afterward, the abstract was read in search of additional information, and if there were still doubts regarding the eligibility of an article, the full text was assessed.

Each journal was searched retrospectively, starting in December 2010 and going back until the beginning of its publication. If no RCTs or SRs were found in 5 consecutive years, handsearching was stopped. Two forms were used, one for recording the results of the handsearch and another for monitoring the reviewed journals. In addition, 2 data extraction forms were designed, one for entering the citation and the type of study (RCT, SR) for each article identified and another for registering the review process of the journals (years and volumes reviewed).

A trained researcher (I.S.) completed a parallel electronic search in the selected journals using MEDLINE (February 2011) through the PubMed search interface (www.pubmed.gov). The search terms "journal name" [Journal] AND (((((“Patient Safety”[Mesh])) AND “Safety Management”[Mesh]) OR “Quality Assurance, Health Care”[Mesh]) AND (“Medical Errors/adverse effects”[Mesh] OR “Medical Errors/prevention and control” [Mesh])) OR “Iatrogenic Disease/prevention and control”[Mesh] were used, limiting type of article to systematic reviews, review, meta-analysis, clinical trial, randomized controlled trial, studies in humans, indexed and with abstract.

Classification and Description of the Studies

Identified studies were entered into a database created in ProCite for Windows, Version 5.0, and were labeled taking into consideration the criteria proposed by the WHO (International Classification for Patient Safety [ICPS]) (1) according to type of incident on patient safety, level of preventive action, (39) specialty and/or service area where the intervention was implemented (Table 2). Level of prevention was defined as follows: (1) primary: measures to prevent the occurrence of a disease or health problem through the control of the causative agents and risk factors; (2) secondary: measures to stop or slow the progression of a disease or of health problems already present in an individual at any point during its course; and (3) tertiary: measures to prevent, delay, or reduce the occurrence of long-term effects from a disease or health problem. Once the studies had been identified and classified according to these criteria, the outcomes evaluated for each study were recorded (Table 2).

Data Collection and Analysis

We entered all the extracted information into an Excel spreadsheet and performed descriptive and comparative analysis for the different outcomes of interest using SPSS for Windows Version 15.0. We established 5-year intervals to study the evolution of the number of studies published. We built 2 x 2 contingency tables to determine the sensibility (percentage of studies identified through MEDLINE) and specificity (percentage of studies not identified through MEDLINE) of the MEDLINE search.

RESULTS

Identification of Publications

A total of 10,162 articles from 787 issues of the 12 selected journals were handsearched, which resulted in the identification of 131 RCTs (1.28%; 131/10,162) and 127 SRs (1.24%; 127/10,162). The parallel electronic search allowed the identification of only 89 of the 131 RCTs and 87 of the 127 SRs retrieved through the handsearch. Thus, the sensitivity of the search in MEDLINE (proportion of studies (RCTs or SRs) retrieved through the MEDLINE search over those identified by handsearching) was 67.9% for RCTs and 68.5% for SRs (Table 3).

Of all the studies identified, 83 RCTs (63.4%, 83/131) and 64 SRs (50.3%, 64/127) assessed the effects of interventions on patient safety. The remaining 48 RCTs (36.6%) and 63 SRs (49.7%) evaluated interventions on road safety, accessibility to health care, health-care management, or economic evaluations, among others. During the period from 1973 to 1992, no RCTs or SRs regarding interventions on patient safety were published in the journals reviewed. The period from 2003 to 2007 had the highest number

Table 2. Incident on Patient Safety and Data Extracted From Studies

Incident on Patient Safety
Clinical administration
Clinical process/procedure
Documentation
Health care-associated infection
Medication/IV fluids (application process, problem)
Blood/blood products
Nutrition
Oxygen/gas/vapor
Medical device/equipment
Behavior
Patient accidents/falls
Infrastructure/building/fixtures
Resources/organizational management
Data extracted from identified studies
Randomized controlled trials
- Year of publication
- Country where the study was conducted
- Scope: primary care, hospital care, other
- Level of prevention: primary, secondary, tertiary
- Type of incident on patient safety
- Specialty and/or service area in which the intervention was implemented
- Number of participants included
- Number of centers: single-center, multicenter h Arms of comparison
- Inclusion criteria
- Setting
- Assigned intervention
- Blinding
- Application of the intervention
- Outcomes assessed
- Methods to assess outcomes
- Sample size calculation
- Cointerventions
Systematic reviews
- Year of publication
- Country where the review was conducted
- Scope: primary care, hospital care, other
- Level of prevention: primary, secondary, tertiary h Type of incident on patient safety
- Specialty and/or service area in which the intervention was implemented
- No. studies included
- Literature search: yes, no, not specified
- Quality assessment of included studies: yes, no, not specified
- Meta-analysis: yes, no

of RCTs published (40 RCTs), the same being true for the period from 2008 to 2010 with respect to SRs (27 in total). The studies were conducted in different countries, the UK being the most productive (23 of the 83 RCTs [27.7%] and 31 of the 64 SRs [48.4%]), followed by the United States (18 of the 83 RCTs [21.7%] and 12 of the 64 SRs [18.7%]), and the Netherlands (13 of the 83 RCTs [15.6%] and 8 of the 64 SRs [12.5%]) (Fig. 1).

Characteristics of the Studies Identified Assessing the Effects of Patient Safety Interventions

Randomized Controlled Trials

Among the 83 RCTs identified, 58 (69.9%) were articles that reported trial results, whereas 25 (30.1%) were protocols. The settings where the studies took place were hospitals (44 RCTs, 53%), primary care centers (38 RCTs, 45.7%), and nursing homes (1 RCT, 1.2%). Most RCTs assessed secondary prevention interventions (59 RCTs, 71%). The types of incidents on patient safety addressed most often were those related to the clinical process/procedure (26 RCTs, 31.3%), documentation (20 RCTs, 24%), resources/organizational management (16 RCTs, 19.3%), medical device/equipment (8 RCTs, 9.6%), and medication/IV fluids (7 RCTs, 8.4%). No RCT assessed incidents on health care-associated infections, blood and derivatives, nutrition, behavior, or infrastructure. A large number of studies were implemented in the area of internal medicine (13 RCTs, 15.6%) and family medicine (12 RCTs, 14.4%). Although 44 RCTs (53%) were performed in one center, 39 RCTs (47%) were multicenter, of which, 17 (20.4%) were performed in more than 10 centers. The studies included a median of 200 participants (range, 29-33,000). Allocation to interventions at the group level (randomization performed by clusters) was reported in 28 RCTs (33.7%). The assigned intervention was described in detail in 80 RCTs (96.4%), whereas the application of the intervention was presented in the 83 studies identified (100%). Most studies (75 RCTs, 90.3%) included 2 arms of comparison. Blinding was used in 25 RCTs, of which, 10 (12%) were double blind, and 15 (18%) were single-blind. In 69 RCTs (83%), the outcomes assessed were specified, and in 79 (91.6%), the method to assess outcomes was provided. Table 4 provides a summary of the main aspects of the RCTs identified.

Systematic Reviews

Of the 64 SRs identified, 47 (73.4%) involved the hospital setting. Thirty (46.8%) assessed secondary prevention interventions, another 30 (46.8%) assessed primary prevention interventions, and only 4 (6.2%) assessed tertiary prevention interventions. The types of incidents on patient safety that were most often included were those related to resource/organizational management (21 SRs, 32.8%), clinical process/procedure (14 SRs, 21.8%), medication/IV fluids (11 SRs, 17.1%), clinical administration (6 SRs, 9.3%), and documentation (6 SRs, 9.3%). No SR assessed incidents on health care-associated

infections, blood and derivatives, nutrition, oxygen, or infrastructure. Most SRs focused on health services research (18 SRs, 28.1%), hospital administration (7 SRs, 10.9%), and public health and preventive medicine (7 SRs, 10.9%). Systematic reviews included a median of 18 studies (range, 3-156). Forty-six SRs (71.8%) reported a literature search, but only 28 (43.7%) described the search period and the databases where the literature search was conducted. Only 16 SRs (25%) reported methodological quality assessments of the included studies. Meta-analysis was performed in 11 SRs (17.1%). Table 4 provides a summary of the main aspects of the RCTs identified.

Table 3. Studies Identified by Handsearching and Electronic Searches in MEDLINE

	Electronic Search (MEDLINE)		
	Yes	**No**	**Total**
Randomized controlled trials			
Handsearch			
Yes	89	42	131
No	0	0	0
Total	89	42	131
Sensitivity: 67.9% (89 RCTs identified through MEDLINE/131 RCTs in total) RCTs not retrieved by MEDLINE search: 32%			
Systematic reviews			
Handsearch			
Yes	87	40	127
No	0	0	0
Total	87	40	127
Sensitivity: 68.5% (87 SRs identified through MEDLINE/127 SRs in total) SRs not retrieved by MEDLINE search: 31.4%			

DISCUSSION

The main objective of our study was to identify and describe RCTs and SRs on the efficacy of interventions in patient safety published in journals that focus on this topic. This allows us to contribute to assess of the current status of the production and publication of these study designs, so common in other areas of healthcare and, therefore, to facilitate the planning of future actions. One of the main strengths of this study is the wide-ranging review conducted, covering 37 years (787 volumes). The handsearch was systematic and exhaustive for all issues and supplements, including letters to the editor, abstracts, and conference presentations, which allowed the identification of all the RCTs and SRs of interventions on patient safety published in specialized journals. This work, however, did not intend to assess the quality of the identified studies, which should be the scope of a future study.

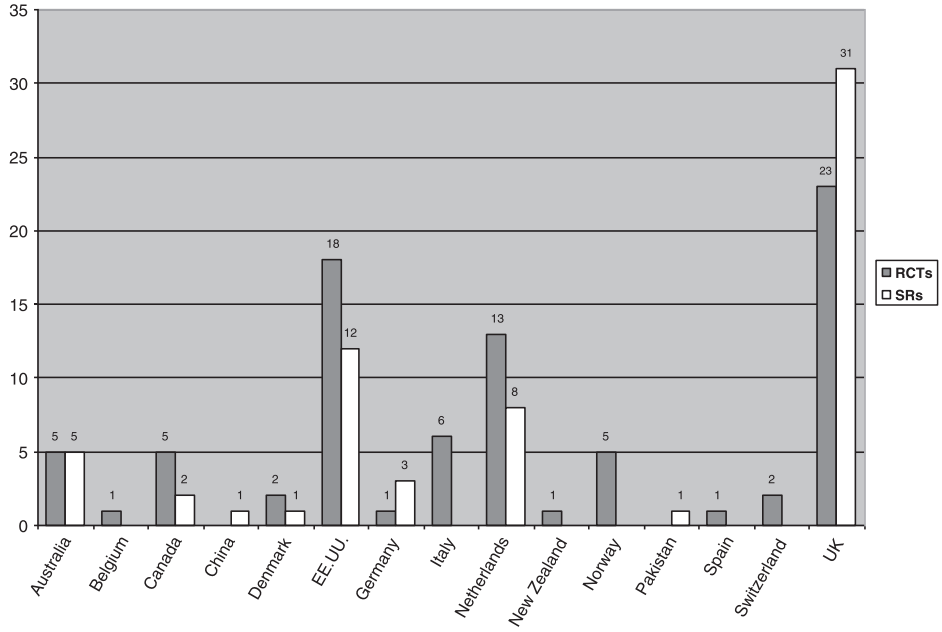

Figure 1. Number of publications on patient safety, per country.

Table 4. Descriptive Characteristics of the Studies Identified on Patient Safety

Randomized Controlled Trials (n=83)		
Setting:	**n**	**%**
- Primary care	38	45.7
- Hospital setting	44	53
- Others(nursing home)	1	1.2
Level of prevention:	**n**	**%**
- Primary	23	27.7
- Secondary	59	71
- Tertiary	1	1.2
Type of patient safety incident:	**n**	**%**
- Clinical administration	3	3.6
- Clinical process/procedure	26	31.3
- Documentation	20	24
- Health care-associated infection	0	0
- Medication/IV fluids	7	8.4
- Blood/blood products	0	0
- Nutrition	0	0
- Oxygen/gas/vapor	1	1.2
- Medical device/equipment	8	9.6

Table 4. Descriptive Characteristics of the Studies Identified on Patient Safety (continued)

- Behavior	0	0
- Patient accidents/falls	2	2.4
- Infrastructure/building/fixtures	0	0
- Resources/organizational management	16	19.3
Specialty and/or service area where the intervention was implemented:	**n**	**%**
- Hospital administration	3	3.6
- Cardiology	8	9.6
- Endocrinology and nutrition	6	7.2
- Gastroenterology	2	2.4
- Geriatrics	8	9.6
- Gynecology	1	1.2
- Research on health services	3	3.6
- Family and community medicine	12	14.4
- Internal medicine	13	15.6
- Preventive medicine and public health	2	2.4
- Pulmonology	6	7.2
- Oncology	5	6
- Orthopedics and traumatology	3	3.6
- Otolaryngology	2	2.4
- Pediatrics	2	2.4
- Psychiatry	6	7.2
- Emergency department	1	1.2
No. participants included in the studies	**Median**	**Range**
	200	29 to 33.000
Number of centers:	**n**	**%**
- One center	44	53
- Multicentric < 10 centers	22	26.5
- Multicentric > 10 centers	17	20.5
Comparison arms:	**n**	**%**
- 2 arms	75	90.3
- 3 arms	7	8.4
- 4 arms	1	1.2
Systematic reviews (n=64)		
Setting:	**n**	**%**
- Primary care	12	18.7
- Hospital setting	48	75
- Others (nursing home, community medicine)	4	6.2
Level of prevention:	**n**	**%**
- Primary	30	46
- Secondary	30	46

Table 4. Descriptive Characteristics of the Studies Identified on Patient Safety (continued)

- Tertiary	4	6
Type of patient safety incident:	**n**	**%**
- Clinical administration	6	9.3
- Clinical process/procedure	14	21.8
- Documentation	6	9.3
- Health care-associated infection	0	0
- Medication/IV fluids	11	17.1
- Blood/blood products	0	0
- Nutrition	0	0
- Oxygen/gas/vapor	0	0
- Medical device/equipment	2	3.1
- Behavior	3	4.6
- Patient accidents/falls	2	3.1
- Infrastructure/building/fixtures	0	0
- Resources/organizational management	21	32.8
Specialty and/or service area where the intervention was implemented:		
- Hospital administration	7	10.9
- Angiology and vascular surgery Cardiology	1	1.5
- General surgery	2	3.1
- Endocrinology and nutrition	2	3.1
- Geriatrics	3	4.6
- Gynecology	1	1.5
- Research on health services	18	28.1
- Family and community medicine	2	3.1
- Internal medicine	2	3.1
- Preventive medicine and public health	7	10.9
- Pulmonology	1	1.5
- Neurology	1	1.5
- Obstetrics	2	3.1
- Ophthalmology	1	1.5
- Oncology	4	6.2
- Orthopedics and traumatology	1	1.5
- Pediatrics	2	3.1
- Psychiatry	3	4.6
- Urology	1	1.5
No. studies included	**Median**	**Range**
	18	3 to 156
Literature search:	**n**	**%**
- Yes	46	71.8
- No	18	28.2

Table 4. Descriptive Characteristics of the Studies Identified on Patient Safety (continued)

Evaluation of the quality of the studies included:	**n**	**%**
- Yes	16	25
- No	48	75
Meta-analysis:	**n**	**%**
- Yes	11	17.1
- No	53	82.8
Main aspects assessed in each RTC:	No. Articles That Fulfill Requirement	
	Yes (%)	**No (%)**
- Inclusion criteria	78 (94)	5 (6)
- Setting	68 (82)	15 (18)
- Assigned intervention	80 (96.4)	3 (3.6)
- Double-blind	10 (12)	58 (70)
- Single-blind	15 (18)	0 (0)
- Application of the intervention	83 (100)	0 (0)
- Primary and secondary outcomes	69 (83)	14 (17)
- Methods to assess outcomes	76 (91.6)	7 (8.4)
- Sample size calculation	61 (73.5)	22 (26.5)
- Groups comparable at baseline	59 (71)	24 (29)
- Detailed demographic characteristics	60 (72.3)	23 (27.7)
- Lack of cointervention	46 (55.4)	37 (44.6)

Despite the observed increase in the number of publications on patient safety, (17) the number of RCTs and SRs that end up being published in journals that focus on this topic is still scarce. In the 37-year period analyzed (1973-2010) (38 years in total), we identified only 131 RCTs and 127 SRs, which amounts to about 3.5 RCTs and 3.4 SRs per year.

It was confirmed that there is a significant number of RCTs and SRs identified only by handsearching and that were not detected by searching through MEDLINE (42 RCTs, 32%, and 40 SRs, 31.4%). This proves, again, the limitations of documental searches carried out exclusively by electronic means, (25-30,34,40) given that it entails the loss of at least one- third of the RCTs and SRs published on patient safety journals. Despite the fact that many journals have been indexed in databases and that, consequently, many RCTs and SRs can be identified through electronic searches, there are still serious problems related to the incorrect indexation of bibliographic databases, even for RCTs and SRs. This limitation must be taken into consideration when conducting electronic searches.

Handsearching plays an important role in the identification of RCTs reports that may be included in SRs on interventions in health care, especially in the identification of RCTs reported as abstracts and letters to the editor, and that are published in languages other than English. The Cochrane Central Register of Controlled Trials (CENTRAL) remains in good standing, thanks to the handsearch of medical literature, given that the Cochrane Review Groups (CRGs) in each country are responsible for coordinating the search of specialized medical literature in their areas of interest. Until now, more than 3000 journals have been or are currently being reviewed through handsearching. Theoretically, handsearching allows the identification of all the literature available. Therefore, combining it with an electronic search is the most comprehensive approach to identify RCTs reports, (25-29,40) which is the best strategy to reduce publication bias. (40)

Although many of the studies identified did not describe in detail the methodology that was used or that some reports were incomplete, we were able to determine their main features. Most RCTs and SRs are centered on the hospital setting. Approximately 71% of RCTs and 47% of SRs assessed secondary prevention interventions, which shows that emphasis has not been placed on preventing patient safety incidents (which are primary prevention interventions, i.e., education on potential risks of accidents in hospitals or control of risk factors for infectious diseases) but rather on hindering or delaying the progression of an incident to causing harm. The types of incidents on patient safety that were more often studied in RCTs and SRs were those related to the clinical process/procedure, documentation, and resources/organizational management. The studies (RCTs, SRs) that evaluated incidents on medication, medical devices, clinical administration, and patient accidents were scarce. No RCTs or SRs evaluated incidents on health care-associated infections, blood and derivatives, nutrition, or infrastructure. The studies were related to different medical specialties or service areas, especially with internal medicine, family and community medicine, and research on health services.

We detected a low or null number of RCTs and SRs published on the effect of interventions to improve medication safety, the handling of blood and derivatives, nosocomial infections, and accidents in patients. This contradicts the recommendations of the WHO on the need to prioritize and encourage research on these topics, which are crucial to patient safety. (2) The above evidence may reflect an insufficient development of investigation in this area or that an undetermined number of RCTs and SRs on patient safety interventions were published in journals of other medical specialties or of general medicine. They could also have been available in journals not published in English. We consider this possibility should be explored in future studies that cover the entire medical literature using handsearching. On the other hand, it should also be noted that studies that evaluate the effects of interventions on patient safety often have methodological peculiarities and that, generally, these interventions are complex. (19,41) Such is the case of the identified studies. Most RCTs were not blinded (58%) or

were single blind (18%), which is due to the fact that many of the interventions assessed did not allowed blinding. Despite the fact that there are other designs that are valid for the evaluation of interventions in patient safety, the RCT remains the study of choice because of the thoroughness with which it must be conducted and the low risk of bias associated to its results. (2,16-19) It was also observed that there is a significant need to increase the production of SRs on the efficacy of interventions on patient safety, given that SRs provide an exhaustive overview of the best available evidence. However, the complexity of patient safety interventions and of the designs used to assess their effects makes it difficult to complete these SRs. The traditional guidelines to perform SRs, such as the Cochrane Handbook, (42) usually focus on the assessment of the effects of pharmacological interventions. (41) These and other factors call for the adaptation of the traditional methods used in clinical research to generate evidence on patient safety. (2,18,19,38)

One of the limitations of this study is that eligibility of the included studies was not evaluated by peer independent reviewers, which could diminish the reliability of the results and increase the risk of subjective bias. Another limitation is that it is restricted to journals published in English, which prevents us from evaluating the efficacy of the searches in non-English journals and the identification of studies published in them. Moreover, we did not evaluate the quality of the studies identified, which we expected to do in the future.

For future research, it would be interesting to identify RCTs and SRs published in non-English journals. Similar works that explore the publication of studies on the efficacy of interventions in patient safety in journals of other medical specialties and in journals of general medicine should also be carried out. In addition, it would be important to take into consideration study designs different from RCTs, which would give us a broader perspective of the current status of research on patient safety.

CONCLUSIONS

The number of RCTs and SRs on interventions to improve patient safety published in journals related to this topic remains limited. Handsearching is indispensable for the identification of all RCTs and SRs available. Having this information promotes a reduction of publication bias, which is essential for conducting systematic reviews, while facilitating the planning process of future research. Further investigation is required to identify all published studies on patient safety interventions, including more journals published in major languages, whether they focus on this or other medical fields.

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SECTION 3

ASSESSMENT OF PERIOPERATIVE SAFETY IN COLOMBIA

Chapter 2

Validation and Psychometric Properties of the Latin-American Spanish Version of the Hospital Survey on Patient Safety Culture Questionnaire in the Surgical Setting

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Submitted

ABSTRACT

Background

The Hospital Survey on Patient Safety Culture (HSPSC) was designed to assess staff views on patient safety in a hospital and has been translated and validated into several languages and populations. However, it is unknown whether safety culture dimensions can be transferred exclusively to surgical settings. This aim herein was to examine the psychometric properties of a Latin-American Spanish version of the HSPSC for its applicability in surgical settings.

Methods

After translation and adjustments, a web-based questionnaire was administered to 150 health care personnel at operating room in a public university-affiliated hospital in Colombia. Descriptive statistics, internal reliability, confirmatory and exploratory factor analysis, and inter-correlations among survey composites were calculated.

Results

The original 12-factor survey is not applicable in its original form. For most of the factors, internal consistency was poor and unacceptable with a Cronbach's $\alpha < 0.5$. Rather, a 9-factor, 36-item instrument showed acceptable factor loadings, internal consistency, and psychometric properties. Five factors were formed with minor changes respecting the original HSPSC. Adjusted factors emerged, like "staffing and work pressure" and "supervisor/manager expectations and actions promoting patient safety", "organizational learning – continuous improvement", and "hospital management support for safety", as well as "repeated errors and perception of safety". Internal consistency for each remaining composite met or exceeded a Cronbach's α value of 0.60. Most inter-correlations were statistically significant.

Conclusions

Psychometric analyses provided overall support for nine of the 12 initial composites of patient safety culture and 36 of the 42 initial questions. We provide the first validated HSPSC-tool for Latin America, specifically for surgical settings and hope to stimulate, hereby, its broader introduction to the clinical practice in this part of the world.

Keywords

prevention, patient safety, HSPSC, operating room

BACKGROUND

The safety culture of an organization is the product of individual and group values, attitudes, perceptions, competencies, and behavioral patterns that determine the commitment to the style and proficiency of an organization's health and safety management. [1] Patient safety is an essential component of healthcare quality; however, even with continuous alertness, health care providers face many challenges in today's healthcare environment in trying to keep patient management in a safe way.

Studying patient safety related topics can provide feedback to the healthcare systems with the possibility of implementing improvement measures based on the identification of specific problems at different areas.[2] The climate of patient safety can be measured as a surrogate and analyzed at different levels of the healthcare system, through identifying strengths and weaknesses that configure the way that healthcare professionals think, behave and approach their work.

A study involving 58 hospitals from five Latin American countries found an estimated prevalence of adverse events in 10.5% of the cases. Six percent of these events were associated with the patient's death and over 28% caused disability. Almost 60% of the total group of adverse events was avoidable. In that sense, working on prevention and encouraging a strong patient safety culture is fundamental to promote and support quality of care among health professionals.[3]

Considering the inherent risks due to the logistic challenges and invasiveness of the procedures performed, operating rooms are particularly challenging for patient safety. Unsafe surgery causes 7-million complications, resulting in 1-million deaths globally each year.[4] Several campaigns and interventions to improve patient safety in surgery have been introduced, including additional checks to confirm procedures, perioperative checklists, communication strategies, and new policies to govern the OR.[4–6] Nevertheless, collecting data on medical errors during surgery is difficult because (near) misses are often underreported or considered unavoidable complications. By using a valid and reliable measurement instrument, culture data can serve as a benchmark for hospitals to assess their performance in advancing the patient safety agenda. The Institute of Medicine states that if a safety culture exists where adverse events can be reported without people being blamed, they have the opportunity to learn from their mistakes and it is possible to make improvements to prevent future human and system errors and, thus, promote patient safety.[7,8]

Healthcare organizations may conduct safety culture assessments for a variety of reasons. Culture assessments can be used to identify areas for improvement, get a baseline and raise awareness about patient safety; secondly, to evaluate patient safety interventions or programs and track change over time; thirdly, to conduct internal and external benchmarking; and finally, to fulfill directives or regulatory requirements, like accredita-

tion standards.[1,9] Interest in safety culture measurement in healthcare organizations has grown in parallel with the increased focus on improving patient safety. To transform culture, it is important to first measure and analyze it. Culture assessment tools create awareness and provide an understanding to develop an action plan to improve patient safety, more important in countries with limited resources.[10]

The Hospital Survey on Patient's Safety (HSPSC) by the Agency for Healthcare Research and Quality (AHRQ) consists of 42 questions and measures 12 dimensions. It was developed by Westat, under contract with AHRQ, with questions derived from a review of existing safety culture literature and instruments, including the Veterans Health Administration's Patient Safety Questionnaire and the Medical Event Reporting System for Transfusion Medicine.[11] The AHRQ instrument was piloted in 20 hospitals and the results were used to generate a list of 12 factors, which displayed high internal consistency through factor analysis (0.63 to 0.84).[12] It is being used in the US and the UK. Several countries have been using translated and validated versions of the HSPSC questionnaire.[7,13–22]

After translating a questionnaire into another language and applying it in a different setting, it is important to check its validity and reliability. Cross-country comparisons are possible, only if the psychometric properties of the validated and translated versions of the HSPSC are comparable to the original structure. To the best of our knowledge, this is the first study developed to explore the surgical safety climate in a Latin American country.

The current study sought to validate a Latin-American Spanish version of the AHRQ Hospital Survey on Patient's safety questionnaire (HSPSC-LA) in a surgical setting. To this aim, we assessed psychometric properties, face validity, content validity, construct validity, and reliability of a Latin-American Spanish version of HSPSC.

METHODS

Design and study population

A cross-sectional study was carried out between 2016 and 2017 at the operating room (OR) in Hospital Universitario San José (HUSJ), a third-tier public university-affiliated hospital in the city of Popayán, Colombia. Popayán is the capital and main city of the department of Cauca; in 2010, it had an estimated population of 270,000 inhabitants and its main medical center is HUSJ. This hospital performs 11,000 surgical procedures per year, primarily in general surgery, orthopedics, gynecology/obstetrics, and plastic surgery.[23,24]

All healthcare providers and OR personnel involved in the perioperative process were included involving medical and non-medical staff (159 members). We collected all study data after the working hours.

After initial validation process, the HSPSC-LA was adapted to a computerized web-based response method arranged that every question had to be answered. Each member of the OR was invited to voluntarily participate in the study and fill out the web-based questionnaire, allowing for confidentiality and anonymity. The questionnaire did not ask for any personal identification data during the survey (neither name of identification details). The research protocol was approved by the ethics committee (Approval act 004, 16-03-2016) and had institutional permission. In addition, the questionnaire asked for direct consent from the participants. Incentives to complete the survey were not provided.

Questionnaire

Background variables

Work-related information and primary work area were not included in this study because all the participants were active OR members. Other related variables collected included how long they had been working in this OR, how many hours a week, and in which function.

Items on patient safety culture

The original HSPSC contains 42 items organized in 12 dimensions.[11] Most items on patient safety culture can be answered by using a five-point scale reflecting the agreement rate: from 'strongly disagree' (1) to 'strongly agree' (5), with a neutral category 'neither' (3). Other items can be answered by using a five-point frequency scale from 'never' (1) to 'always' (5). In addition, there are two mono-item outcome variables, ie., 1) Patient safety grade, measured with a five-point scale from 'excellent' (1) to 'failing' (5); and 2) Number of events reported, how often the respondent has submitted an event report in the past 12 months (answer categories: 'none'; '1–2 event reports'; '3–5 event reports'; '6–10 event reports'; and '11–20 event reports') (Table 1).

Translation process

Before starting the validation process, we considered a previous translation and validation into Spanish (Castilian from Spain) developed by the Sistema Nacional de Salud Español [19]. The available version of the HSPSC translated into Spanish was revised in detail. Some items were incomprehensible in Latin-American Colombian Spanish and others had translation issues due to cultural and environmental differences.

Therefore, we translated the original survey into Latin-American Colombian Spanish by following the AHRQ guidelines for translating surveys on patient safety culture

Table 1. Factors and items of the original version of the AHRQ-HSPSC.

Factor	Dimensions	Questions*
1	Teamwork Within Units	A1, A3, A4, A11
2	Supervisor/Manager Expectations & Actions Promoting Patient Safety	B1, B2, B3n, B4n
3	Organizational Learning - Continuous Improvement	A6, A9, A13
4	Management Support for Patient Safety	F1, F8, F9n
5	Overall Perceptions of Patient Safety	A10n, A15, A17n, A18
6	Feedback & Communication About Error	C1, C3, C5
7	Communication Openness	C2, C4, C6n
8	Frequency of Events Reported	D1, D2, D3
9	Teamwork Across Units	F2n, F4, F6n, F10
10	Staffing	A2, A5n, A7n, A14n
11	Handoffs & Transitions	F3n, F5n, F7n, F11n
12	Nonpunitive Response to Errors	A8n, A12n, A16n
Mono-item	Patient Safety Grade	Excellent, Very Good, Acceptable, Poor, Failing
	Number of Events Reported	

*n represents negatively worded questions.

and combined those results with the previous Spanish version.[25] These guidelines propose a team approach based on current best practices for survey translations.[25,26] To develop a well-translated HSPSC-LA, the original survey was translated into Latin-American Spanish, then it was compared and adjusted with the Spanish version and, finally, translated back into English. The entire process was done by a research team, along with a bilingual translator with professional work experience in developing surveys. Environmental, cultural, and local issues present in the questions were actively discussed by the team to reach consensus.

Face and content validity

We investigated the face and content validity of the HSPSC-LA. To obtain face validity, a group of advisors: three physicians and three nurses from the HUSJ conducted an initial review of the questionnaire. They met to review the translation, suggested changes, and decided on the most suitable translation. Thereafter, based on consensus with the research team, together determined whether the questions from the pre-final HSPSC-LA version suited the Colombian culture and if the format of the questions was conceptually equivalent to the original English questions (content validity). All information gathered was used to prepare the final version of the HSPSC-LA (Online Appendix).

Data screening and pre-analyses

Completeness of the data was verified. Nine respondents were excluded from the analyses because they had not fully completed the questionnaire. Only responses without missing data were analyzed.

We checked whether the inter-item correlations were sufficient through an examination of the correlation matrix. Questions belonging to the same underlying dimension will correlate, given that they measure the same aspect of patient safety culture. Items that do not correlate, or correlate with only a few other variables, are not suited for factor analysis.[27] Bartlett's test demonstrated that the inter-item correlations were sufficient: $\chi 2 = 2920.2$; $df = 861$; $p < 0.001$.

We also checked whether the opposite occurred: too much correlation between the items. Ideally, every aspect of patient safety culture uniquely contributes towards the concept of patient safety culture. A high correlation between two items means that patient safety culture aspects overlap to a large extent. The overlap in the answer patterns is about 50% when a correlation is 0.7.[27]

In addition, the Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy was determined. This value can range from 0 to 1. A value near 1 indicates hardly any spread in the correlation pattern, enabling reliable and distinctive dimensions by factor analysis.[20] The KMO score was 0.81 above Kaiser's criterion of 0.5. These pre-analyses demonstrated that the data could be suitable for factor analysis.

Data analysis

Factor analysis defines which items are closely linked and refer jointly to an underlying dimension (or factor). Thus, the items can be reduced to the smallest possible number of concepts that still explain the largest possible part of the variance. In line with other validation related studies,[7,15–18] a confirmative factor analysis was performed (principal component analysis with oblique rotation) to investigate whether the factor structure of the original questionnaire can be used with Latin-American data.

The data were also studied with explorative factor analysis (principal component analysis with maximum likelihood approach) to examine whether another composition of items and factors would best fit the data. When establishing the number of factors, initially the eigenvalue (eigenvalue > 1: Kaiser's criterion) was taken into account, besides the extent of variance explained, the shape of the scree plot and the possibility of interpreting the factors. Then, an oblique rotation was performed to determine which items loaded most highly on which factor. Using a conservative approach, an item was considered to have sufficient contribution to the particular factor if its loading was ≥0.4. Items with low-factor loadings (<0.4) or cross-loading on multiple factors (>0.3) were removed. Finally, factor analysis was conducted on the subset of items retained.

The internal consistency of the factors was calculated with Cronbach's alpha (α), a value between 0 and 1. If different items are supposed to measure the same concept, the internal consistency (reliability) should be greater than or equal to 0.6.[27] Given that the questionnaire contains positively and negatively worded items, the negatively formulated items were first recoded to make sure that a higher score always means a more positive response.

Construct validity was studied by calculating scale scores for every factor and, subsequently, calculating Pearson correlation coefficients between the scale scores. The construct validity of each factor is reflected in moderately related scale scores. High correlations ($r > 0.7$), however, would indicate that factors measure the same concept and these factors may be combined and/or some items could be removed. In addition, correlations of the scale scores were calculated with the outcome variable: patient safety grade.

Data was summarized as proportions, means, and SD values considering their distribution. T tests were applied to compare the mean values, and $p < 0.05$ was considered statistically significant. For each positively worded item, the proportion of positive responses was calculated, that is, the percentage of respondents answering the question by checking "strongly agree" and "agree" or "always" and "most of the time".[11] All statistical analyses were performed by using SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.

RESULTS

All 159 members from the OR were asked to participate from March 2016 to May 2017 and 150 completed the survey. Nine participants (all temporary personnel) did not complete the questionnaire and were excluded from the analysis. We did not identify missing data. Therefore, 150 participants yielded a 94% response rate.

Confirmatory factor analysis

The 12 dimensions resulting from the factor analysis of the AHRQ have already been mentioned. Items forming one factor in the AHRQ study have been studied in 12 separate factor analyses, to see whether a group of items also loaded on one factor with the Latin-American data. The internal consistency was calculated for every factor and compared with the internal consistency found in the original US study (Table 2).

For each factor, the internal consistency of the Latin-American items was lower than that of the original items in the AHRQ study, except for Teamwork within units, Frequency of event reporting, and Feedback and communication about errors, which was very close. For the majority of factors, the internal consistency was poor and unacceptable with Cronbach's $\alpha < 0.5$ (Table 2). This led to carrying out an exploratory factor analysis to investigate if a factor structure exists that best fits the Latin-American data.

Table 2. Characteristics of the factors after initial confirmatory factor analysis

Factor	No. of items	Items / Questions	Cronbach's α US data	Cronbach's α Latin American data
Teamwork within units	4	A1, A3, A4, A11	0.83	0.78
Frequency of event reporting	3	D1, D2, D3	0.84	0.78
Feedback and communication about errors	3	C1, C3, C5	0.78	0.78
Organisational learning and continuous improvement	3	A6, A9, A13	0.76	0.66
Nonpunitive response to error	3	A8, A12, A16	0.79	0.67
Supervisor/manager expectations/actions	4	B1, B2, B3, B4	0.75	0.68
Staffing	4	A2, A5, A7, A14	0.63	0.53
Hospital handoffs and transitions	4	F3, F5, F7, F11	0.80	0.77
Teamwork across hospital units	4	F2, F4, F6, F10	0.80	0.71
Hospital management support for safety	3	F1, F8, F9	0.83	0.72
Communication openness	3	C2, C4, C6	0.72	0.54
Overall perceptions of safety	4	A10, A15, A17, A18	0.74	0.48

Exploratory factor analysis

After analyzing the initial correlation matrix, we excluded one item (C6) due to poor inter-correlations (<0.3) with all items. Eleven factors were drawn by exploratory factor analysis (eigenvalues > 1.0). Two were deleted because one did not include items after rotation and another only contained one item. Five items had low factor loadings (<0.4) and were not included in the final structure (A15, A17, F2, F4, C4). Finally, a version with 9 factors and 36 items was the best solution that explained 60.5% of the variance in the responses. Table 3 shows the factor loadings after rotation.

Internal consistency was calculated for every factor (Cronbach's α). Overall, it was variable ($0.60 < \alpha < 0.84$), but all the HSPSC-LA factors have values above 0.6 (Table 3).

One of the 9 factors was similar to the original HSPSC questionnaire: "Frequency of events reported" (Cronbach's $\alpha = 0.78$). Four factors were used as in the original with the addition of one item to each: "Teamwork within units" (A2) (Cronbach's $\alpha = 0.77$), "Non-punitive response to errors" (A7) (Cronbach's $\alpha = 0.66$), "Hospital handoffs and transitions" (F6) (Cronbach's $\alpha = 0.80$), "Feedback and communication about errors" (C2) (Cronbach's $\alpha = 0.80$).

One factor was adjusted containing two original items in addition to two new ones. It was titled: "Staffing and work pressure" (B3, F9) (Cronbach's $\alpha = 0.72$). One factor, "Supervisor/Manager expectations & actions promoting patient safety" was created with less items than the original (Cronbach's $\alpha = 0.74$).

The factors, "Organizational learning – Continuous improvement" and "Hospital management support for safety" were brought together to a single new factor labelled

"Organizational learning, continuous improvement, and hospital support for safety" including seven items (Cronbach's α = 0.84). Finally, item A10 – included in the original factor, "Overall perceptions of safety" – was combined with B4 and named "Repeated errors and perception of safety" (Cronbach's α = 0.60)".

Table 3. Characteristics of the HSPSC-LA factors after exploratory factor analysis

Factor/Items and Cronbach's α	1	2	3	4	5	6	7	8	9
Factor 1. Organizational learning, continuous improvement, *and hospital support for safety* (α = 0.77)*									
F8. Actions of hospital management show that patient safety is a top priority.	0.706								
A9. Mistakes have led to positive changes here.	0.646								
F10. Hospital units work well together to provide the best care for patients.	0.622								
A13. After we make changes to improve patient safety, we evaluate their effectiveness.	0.584								
A18. Our procedures and systems are good at preventing errors from happening.	0.557								
F1. Hospital management provides a work climate that promotes patient safety.	0.533								
A6. We are actively doing things to improve patient safety.	0.471								
Factor 2. Hospital handoffs and transitions (α = 0.80)									
F11n. Shift changes are problematic for patients in this hospital.		0.746							
F7n. Problems often occur in the exchange of information across hospital units.		0.692							
F5n. Important patient care information is often lost during shift changes.		0.600							
F6n. It is often unpleasant to work with staff from other hospital units.		0.562							
F3n. Things "fall between the cracks" when transferring patients from one unit to another.		0.537							
Factor 3. Staffing *and work pressure* (α = 0.72)									
A14n. We work in "crisis mode," trying to do too much, too quickly.			0.616						
B3n. Whenever pressure builds up, my supervisor /manager wants us to work faster, even if it means taking shortcuts.			0.553						
A5n. Staff in this unit work longer hours than is best for patient care.			0.525						
F9n. Hospital management seems interested in patient safety only after an adverse event happens.			0.488						
Factor 4. Teamwork within units (α = 0.77)									
A1. People support one another in this unit.				0.757					
A3. When a lot of work needs to be done quickly, we work together as a team to get the work done.				0.712					

Table 3. Characteristics of the HSPSC-LA factors after exploratory factor analysis (continued)

Factor/Items and Cronbach's α	1	2	3	4	5	6	7	8	9
A4. In this unit, people treat each other with respect.				0.606					
A11. When one area in this unit gets really busy, others help out.				0.518					
A2. We have enough staff to handle the workload.				0.423					
Factor 5. Nonpunitive response to error (α = 0.66)									
A12n. When an event is reported, it feels like the person is being written up, not the problem.					0.571				
A16n. Staff worry that mistakes they make are kept in their personnel file.					0.569				
A8n. Staff feel like their mistakes are held against them.					0.494				
A7n. We use more agency/temporary staff than is best for patient care.					0.448				
Factor 6. Feedback and communication about error (α = 0.80)									
C2. Staff will freely speak up if they see something that may negatively affect patient care.						0.687			
C3. We are informed about errors that happen in this unit.						0.655			
C1. We are given feedback about changes put into place based on event reports.						0.596			
C5. In this unit, we discuss ways to prevent errors from happening again.						0.442			
Factor 7. Frequency of events reported (α = 0.78)									
D3. When a mistake is made that could harm the patient, but does not, how often is this reported?							0.960		
D2. When a mistake is made, but has no potential to harm the patient, how often is this reported?							0.631		
D1. When a mistake is made, but is caught and corrected before affecting the patient, how often is this reported?							0.416		
Factor 8. Supervisor/Manager expectations & actions promoting patient safety (α = 0.74)									
B1. My supervisor/manager says a good word when he/she sees a job done, according to established patient safety procedures.								0.939	
B2. My supervisor/manager seriously considers staff suggestions for improving patient safety.								0.483	
Factor 9. Repeated errors and perception of safety (α = 0.60)									
A10n. It is just by chance that more serious mistakes don't happen around here.									0.493
B4n. My supervisor/manager overlooks patient safety problems that happen over and over.									0.472

* Underlines represent modifications of the Factor's titles from the original.

Table 4 presents the correlation between mean values, scale scores, and intercorrelations among factors prepared to assess construct validity. The highest correlations were those between Factor 1 and Factor 6 (r = 0.547), but no exceptionally high correlations were noted. The highest correlation with patient safety grade was for the factor, "Organizational learning, continuous improvement, and hospital support for safety" (r = 0.492).

Table 4. Mean values, correlation with patient safety grade and intercorrelations of the factors

Factor	Mean	SD	Patient safety grade	1	2	3	4	5	6	7	8	9
Factor 1. Organizational learning, continuous improvement, and hospital support for safety	3.62	0.63	0.492	1								
Factor 2. Hospital handoffs and transitions	3.12	0.71	0.392	0.421	1							
Factor 3. Staffing and work pressure	2.95	0.80	0.382	0.388	0.446	1						
Factor 4. Teamwork within units	3.53	0.65	0.347	0.520	0.232	0.376	1					
Factor 5. Nonpunitive response to error	2.96	0.73	0.223	0.126*	0.325	0.452	0.265	1				
Factor 6. Feedback and communication about error	3.19	0.81	0.445	0.547	0.316	0.334	0.334	0.243	1			
Factor 7. Frequency of events reported	3.21	0.80	0.369	0.471	0.245	0.247	0.251	0.159*	0.495	1		
Factor 8. Supervisor/Manager expectations & actions promoting patient safety	3.35	0.87	0.348	0.412	0.199	0.406	0.400	0.203	0.402	0.266	1	
Factor 9. Repeated errors and perception of safety	3.51	0.81	0.261	0.274	0.337	0.410	0.343	0.385	0.192	0.172	0.171	1

Note. All correlations were below r^2=0.7. Correlation between Factors 2 and 8, 5 and 8, 6 and 9, 7 and 9, and 8 and 9 are significant at $p < 0.05$. The remaining correlations are significant at $p < 0.01$. *Not significant.

Survey findings

In all, 84 medical doctors participated (n = 84, 56%) including specialists (n = 51), residents (n = 22), and general practitioners (n = 11). In addition, 28 nurses and nursing assistants (19%), 12 surgical assistants (8%), 9 pharmacy personnel (6%), 7 administrative services (4.7%), 7 cleaning personnel (4.7%), and 3 X-ray technicians (2%); 132 (88%) participants had direct contact with patients in the OR.

Healthcare personnel working hours ranged from four to 98 per week; 57 participants (38%) work less than 40 h per week, 60 from 41 to 59 h per week (40%), and 33 more than 61 h per week (22%), (mean = 42 h per week, SD = 20). Length of employment varied,

with 53.3% having worked for 5 years or less at the OR, and 31% having professional experience of 10 years or longer.

The overall patient safety culture score was 79% (SD = 12%). The overall score means were 78±12% for doctors, 83±11% for nurses/nurses assistants, and 68±12% for surgical assistants. Scores were lower in personnel with direct contact with patients at 78%, compared with administrative staff at 84% (MD = -5.6% 95%CI -11% - -5% p = 0.073). There were no relation of patient safety culture score with profession or length of employment.

Over half of the healthcare personnel (62%) have never reported medical errors or incidents relating to patient safety during the last year. All personnel have reported a mean of 2.3 incidents during the last year except doctors with a mean of reporting of 0.8 events and a median of zero (p = 0.002).

The highest percentage of positive responses was obtained by the factors "Teamwork within units" and "Organizational Learning—Continuous Improvement" (70%), whereas the lowest were "Staffing" (37%), "Nonpunitive response to error" (34%), and "Communication openness" (30%).

DISCUSSION

The safety culture environment is considered the most important barrier to improving patient care safety.[28] The starting point for developing a safety culture should be the evaluation of the current culture by using an appropriate, validated, and setting-adjusted instrument.[7,28] This study examined the psychometric properties of the HSPSC-LA. We found that the original US 12-factor survey is not applicable to the Colombian personnel in a surgical setting. Rather, a 9-factor, 36-item instrument showed acceptable factor loadings and internal consistency.

Our results suggest that with appropriate translation into Latin-American Spanish, slight modifications and adaptation, the HSPSC performs adequately in surgical settings in Colombia. The construct validity was satisfactory for all factors and moderate correlations among them show that no two factors measure the same construct. In addition, all factors correlated positively with the outcome variable patient safety grade. Our findings are consistent with previous studies supporting that the HSPSC requires adaptation and setting adjustments to meet minimum psychometric criteria.[17,29,30]

The internal consistency of the nine factors exhibited good to satisfactory Cronbach's α scores (>0.60). Small shifts of items were noted across factors; two original factor titles were modified to improve their understandability and six questions were excluded from the original HSPSC. These changes could be explained by underlying differences with the original language, cultural environment, and specific setting of use of the questionnaire. This HSPSC-LA version has been developed and evaluated in a surgical setting,

whereas the original one included all areas in hospitals in the US. This could alter the importance of some items that describe interaction among units and teamwork across units.

Five original factors received items from other ones, suggesting a simplification of the original domains in the HSPSC-LA. Internal similarities in personnel from a single hospital area could explain this finding. Original factors "Organizational learning - Continuous improvement" and "Hospital management support for safety" have formed together a single new factor with seven items that seem to be linked. Personnel at hospitals in Colombia consider hospital management and their support as the main source of improvement and information about safety and this may differ in other developed countries.[31–33]

The factor "Supervisor/Manager expectations and actions promoting patient safety" lost question B3, which refers mainly to work pressure and working fast. In the HSPSC-LA, B3 was included with items of "Staffing". We interpret that personnel consider that work pressure is quite related with the number of people available in the OR. This may be the case of this hospital and certainly, limited staff is a situation present in some hospitals in developing countries. This perception is consistent with its potential effect on safe care.[34,35]

A new factor was formed by items B4 and A10. The first one referred to repeated errors by manager/supervisor and the second one to the effect of chance on more serious mistakes. Personnel perceive a close relationship between repetitive errors – as a source of unsafe practices – and the manager/supervisor responsibility in the response to them. Parand et al., systematically reviewed the literature to assess the role of hospital managers in quality and patient safety. They found evidence that managers' time spent and work can influence quality and safety clinical outcomes, processes, and performance at hospital level.[36] In addition, poor relationships between doctors and managers affect staff and patients' care and seem to be associated with the long-term failure of organizations to thrive.[37]

The percentage of positive scores for individual domains were higher than US results.[38] "Teamwork across units" had low positive responses (48%). This agrees with others, suggesting that interaction between units/departments could be perceived as a source of unsafe practices.[39,40] Personnel appeared unhappy to work with colleagues in other units but reported good teamwork within their own units.[18] The OR has strong interactions and communication with areas like intensive care units or the emergency department. Teamwork is a crucial part for the improvement of patient safety, and personnel should be encouraged and supported in their efforts to establish good relationships with people working in other units.[18]

An important finding was the low rate of reporting of incidents. Participants without any report during the past year exceeded 50%. This estimate was lower than the 84%

described in Turkey[18], but much higher than 40% reported in Dutch hospitals.[7] Fear of reprisal in a punitive system has been identified as a determinant of reluctance to report adverse events.[14] Recently, Elmontsri M. et al., presented a systematic review about the status of patient safety culture in Arab countries in which they identified that non-punitive response to error is seen as a serious issue that needs to be improved. Healthcare professionals in Arab countries tend to think that a 'culture of blame' still exists that prevents them from reporting incidents.[41] This situation is similar in Latin America where only few report events and still staff feels that their mistakes and reported events could be used against them, configuring punitive systems.[42,43]

While most individual institution reporting systems would have a limited volume of reports and insufficient power to draw statistically valid conclusions about certain events, they could be valuable to management and educators by identifying problems. Merely one report of a near miss could identify a critical situation and lead to quality improvement.[44] The Iberoamerican study of adverse events (IBEAS study) has enabled us to grasp the situation of patient safety and harmful incidents in certain hospitals in Latin America.[3] Critical areas of improvement detected in this study include 1) implementation of a non-blaming system to report adverse events, 2) enhancement of non-punitive policies with respect to error reporting, 3) promotion of open communication, and 4) promotion of management support of safety culture. However, active reporting has yet to be established in the sector, starting from our health care educational system in which students feel uncomfortable speaking up about patient safety issues and feel lack of confidence in their skills to manage safety risks.[45]

Our results show that administrative staff (without direct patient contact) have a higher perception of safety than those with direct contact. Probably, they look upon care and safety more through their role as potential patients than as care providers and, thus, are less concerned. Although administrative staff are always considered an important part of the safety culture system, studies are scarce regarding their role in perioperative safety.

Self-report instruments are commonly used, although weaknesses are widely recognized. Some tests are long and tedious and respondents simply lose interest and do not answer questions accurately. Additionally, people are sometimes not the best judges of their own behavior and try to hide true feelings, thoughts, and attitudes.[18] In contrast with this approach, we used an online web-based version of the questionnaire with a high rate of completeness compared with previous reports.[13,15,22] Survey response rates have been declining over the past decade and web-based questionnaires could replace traditional paper questionnaires with minor effects on response rates and at lower costs.[46,47] This could be an alternative to improving adherence, preventing bias, and aiding in the practical usefulness of the HSPSC.

There are limitations to consider when interpreting these results. The incomplete transferability of the 12 factors of the original HSPSC remains a limitation to compare with other areas worldwide and the source of those differences is worth discussing. Our findings provide an initial assessment of the participating OR. Further research should include a larger sample size across multiple surgical and perioperative facilities in other Colombian or Latin American hospitals to confirm the underlying structure of the HSPSC-LA in surgical settings. Finally, strong cultural differences could potentially reduce the external validity of our results but not their usefulness. We hypothesize that the main differences in the psychometric properties of this instrument compared with the original HSPSC are not due to language differences but due to the setting in which it is used.

In conclusion, this work provides the first validated surgical HSPSC tool for Latin America and hope to stimulate, hereby, its broader introduction to the clinical practice in this part of the world. Change starts with the feeling of a need to change. This questionnaire could provide a baseline of the surgical safety climate, monitor changes on time, and assess interventions aiming to improve surgical safety culture.

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CONFLICT OF INTEREST STATEMENT

None declared.

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APPENDIX

Table 1. Original HSPSC questionnaire translated to Spanish

Included items	Code
El personal se apoya mutuamente en esta unidad.	A1
Tenemos suficiente personal para hacer todo el trabajo.	A2
Cuando tenemos mucho trabajo, colaboramos todos como un equipo para poder terminarlo.	A3
En esta unidad nos tratamos todos con respeto.	A4
A veces, no se puede proporcionar la mejor atención al paciente porque la jornada laboral es agotadora.	A5
Tenemos actividades dirigidas a mejorar la seguridad del paciente.	A6
En ocasiones no se presta la mejor atención al paciente porque hay demasiado personal temporal.	A7
Si los compañeros o los superiores se enteran de que has cometido algún error, lo utilizan en tu contra.	A8
Cuando se detecta algún fallo en la atención al paciente se llevan a cabo las medidas apropiadas para evitar que ocurra de nuevo.	A9
Es sólo por casualidad que no ocurren errores más serios en esta unidad.	A10
Cuando alguien está sobrecargado de trabajo, suele encontrar ayuda en los compañeros.	A11
Cuando se detecta algún fallo, antes de buscar la causa, buscan un "culpable".	A12
Los cambios que hacemos para mejorar la seguridad del paciente se evalúan para comprobar su efectividad.	A13
Trabajamos bajo presión para realizar demasiadas cosas muy rápidamente.	A14
La seguridad del paciente nunca se sacrifica por hacer más trabajo.	A15
Cuando se comete un error, el personal teme que eso quede en su hoja de vida.	A16
Tenemos problemas con la seguridad de los pacientes en esta unidad.	A17
Nuestros procedimientos y sistemas son efectivos para la prevención de errores en la atención del paciente.	A18
Mi superior o jefe expresa su satisfacción cuando intentamos evitar riesgos en la seguridad del paciente.	B1
Mi superior o jefe tiene en cuenta, seriamente, las sugerencias del personal para mejorar la seguridad de los pacientes.	B2
Cuando aumenta la presión del trabajo, mi superior o jefe pretende que trabajemos más rápido, aunque se pueda poner en riesgo la seguridad del paciente.	B3
En la atención de los pacientes, mi superior o jefe no hace caso de los problemas de seguridad que se repiten una y otra vez.	B4
La Dirección de este hospital brinda un ambiente laboral que promueve la seguridad del paciente.	F1
Las unidades de este hospital no se coordinan bien entre ellas.	F2
La información de los pacientes se pierde cuando éstos se transfieren de una unidad a otra.	F3
Hay buena cooperación entre las unidades del hospital que necesitan trabajar juntas.	F4
Durante los cambios de turno, a menudo se pierde información importante del cuidado del paciente.	F5

Table 1. Original HSPSC questionnaire translated to Spanish (continued)

Included items	Code
A veces es incómodo o desagradable trabajar con personal de otras unidades.	F6
A menudo surgen problemas en el intercambio de información entre unidades de este hospital.	F7
Las acciones de la dirección de este hospital muestran que la seguridad del paciente es una de sus prioridades.	F8
La dirección del hospital sólo se interesa por la seguridad del paciente cuando ya ha ocurrido un evento adverso.	F9
Las unidades del hospital trabajan bien entre ellas para proveer el mejor cuidado para los pacientes.	F10
Surgen problemas en la atención de los pacientes como consecuencia de la entrega de turno.	F11
Cuando notificamos algún incidente, nos informan sobre qué tipo de cambios o ajustes se han llevado a cabo.	C1
Cuando el personal ve algo que puede afectar negativamente a la atención que recibe el paciente, habla de ello con total libertad.	C2
Se nos informa sobre los errores que se cometen en esta unidad.	C3
El personal puede cuestionar con total libertad las decisiones o acciones de sus superiores.	C4
En esta unidad, hablamos sobre formas de prevenir los errores para que no se vuelvan a cometer.	C5
El personal tiene miedo de hacer preguntas cuando algo no parece estar bien.	C6
Se reportan los errores que son descubiertos y corregidos antes de que afecte al paciente.	D1
Cuando se comete un error, pero no tiene el potencial de dañar al paciente, ¿qué tan frecuentemente es reportado?	D2
Cuando se comete un error que pudiese dañar al paciente, pero no lo hace, ¿qué tan a menudo es reportado?	D3

Table 2. HSPSC-LA version of the questionnaire after exploratory factor analysis

Included items	Code
El personal se apoya mutuamente en esta unidad.	A1
Tenemos suficiente personal para hacer todo el trabajo.	A2
Cuando tenemos mucho trabajo, colaboramos todos como un equipo para poder terminarlo.	A3
En esta unidad nos tratamos todos con respeto.	A4
A veces, no se puede proporcionar la mejor atención al paciente porque la jornada laboral es agotadora.	A5
Tenemos actividades dirigidas a mejorar la seguridad del paciente.	A6
En ocasiones no se presta la mejor atención al paciente porque hay demasiado personal temporal.	A7
Si los compañeros o los superiores se enteran de que has cometido algún error, lo utilizan en tu contra.	A8
Cuando se detecta algún fallo en la atención al paciente se llevan a cabo las medidas apropiadas para evitar que ocurra de nuevo.	A9
Es sólo por casualidad que no ocurren errores más serios en esta unidad.	A10
Cuando alguien está sobrecargado de trabajo, suele encontrar ayuda en los compañeros.	A11
Cuando se detecta algún fallo, antes de buscar la causa, buscan un "culpable".	A12
Los cambios que hacemos para mejorar la seguridad del paciente se evalúan para comprobar su efectividad.	A13
Trabajamos bajo presión para realizar demasiadas cosas muy rápidamente.	A14
Cuando se comete un error, el personal teme que eso quede en su hoja de vida.	A16
Nuestros procedimientos y sistemas son efectivos para la prevención de errores en la atención del paciente.	A18
Mi superior o jefe expresa su satisfacción cuando intentamos evitar riesgos en la seguridad del paciente.	B1
Mi superior o jefe tiene en cuenta, seriamente, las sugerencias del personal para mejorar la seguridad de los pacientes.	B2
Cuando aumenta la presión del trabajo, mi superior o jefe pretende que trabajemos más rápido, aunque se pueda poner en riesgo la seguridad del paciente.	B3
En la atención de los pacientes, mi superior o jefe no hace caso de los problemas de seguridad que se repiten una y otra vez.	B4
La Dirección de este hospital brinda un ambiente laboral que promueve la seguridad del paciente.	F1
La información de los pacientes se pierde cuando éstos se transfieren de una unidad a otra.	F3
Durante los cambios de turno, a menudo se pierde información importante del cuidado del paciente.	F5
A veces es incómodo o desagradable trabajar con personal de otras unidades.	F6
A menudo surgen problemas en el intercambio de información entre unidades de este hospital.	F7
Las acciones de la dirección de este hospital muestran que la seguridad del paciente es una de sus prioridades.	F8
La dirección del hospital sólo se interesa por la seguridad del paciente cuando ya ha ocurrido un evento adverso.	F9

Table 2. HSPSC-LA version of the questionnaire after exploratory factor analysis (continued)

Included items	Code
Las unidades del hospital trabajan bien entre ellas para proveer el mejor cuidado para los pacientes.	F10
Surgen problemas en la atención de los pacientes como consecuencia de la entrega de turno.	F11
Cuando notificamos algún incidente, nos informan sobre qué tipo de cambios o ajustes se han llevado a cabo.	C1
Cuando el personal ve algo que puede afectar negativamente a la atención que recibe el paciente, habla de ello con total libertad.	C2
Se nos informa sobre los errores que se cometen en esta unidad.	C3
En esta unidad, hablamos sobre formas de prevenir los errores para que no se vuelvan a cometer.	C5
Se reportan los errores que son descubiertos y corregidos antes de que afecte al paciente.	D1
Cuando se comete un error, pero no tiene el potencial de dañar al paciente, ¿qué tan frecuentemente es reportado?	D2
Cuando se comete un error que pudiese dañar al paciente, pero no lo hace, ¿qué tan a menudo es reportado?	D3

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SECTION 4

PREOPERATIVE AND INTRAOPERATIVE ANESTHETIC INTERVENTIONS FOCUSED ON QUALITY AND SAFETY

Chapter 3

Ultrasound guidance for central venous catheterisation. A Colombian national survey.

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Int J Qual Health Care 2018;30(8):649–653.

ABSTRACT

Quality problem or issue

Ultrasound (US) is a widely propagated medical technology. Anaesthesiologists increase procedural safety by using US techniques, but training and availability are essential for its usage. Although its utility for central venous catheterisation (CVC) is well established, only a paucity of evidence is available regarding its use in low- and middle-income countries. This study is a nationwide survey of Colombian anaesthesiologists designed to explore the current use of US guidance for CVC.

Initial assessment and implementation

Web-based survey at National level. Anaesthesiologists registered in the Colombian Society of Anaesthesiology and Resuscitation database.

Choice of solution

Demographic variables (age and gender), anaesthesia expertise, years of anaesthesiology practice, US availability, use of US during CVC, reasons for not using US and training experience were collected.

Evaluation

Of 351 respondents (12.3% response rate), 45% reported using US sometimes and always for CVC (95% CI 39%–50%) (n = 157). Most anaesthesiologists obtained training in US through external courses (50.4%) or from colleagues (22.8%). Of the total respondents, 62.7% (n = 220) have US equipment available at all time and this factor was independently associated with the use of US for CVC (adjusted odds ratio [OR] = 38.6, $P < 0.001$).

Lessons learned

US guidance is not a common technique used for CVC by Colombian anaesthesiologists; an important barrier for its use is lack of equipment.

Keywords

ultrasound, central venous catheterisation, patient safety

QUALITY PROBLEM OR ISSUE

Introduction of ultrasound (US) in the medical practice has shown several benefits in the safety of numerous procedures [1]. US-guided insertion of central venous catheter has become a highly recommended or even mandatory technique, according to several guidelines and protocols of venous catheterisation [1]. In 1984, Legler et al. [2] used the Doppler technique (ultrasonic Doppler, doppler study or evaluation) to guide jugular venous catheterisations. Two years later, Yonei et al. [3], used 2D-US to insert central venous catheters. Since then, this technique has improved in terms of precision, safety and availability for healthcare workers.

CVC is a common procedure performed by anaesthesiologists and many physicians in the emergency department and intensive care units [1]. US has proven to be a good complementary strategy for CVC because of a great number of benefits, like increased success rates [1, 4], reduced number of attempts and shorter time required to perform the procedure compared with a landmark technique [4, 5] and lessened complications (e.g. malposition, lung or vascular injuries, pneumothorax and thrombosis) [5–7].

Because of these advantages, several medical organisations and government agencies advocate the use of this technique and encourage its propagation across all healthcare centres [8–12]. Despite these recommendations, many limitations and barriers still exist for US to become a universal technique for CVC and other anaesthesia-related procedures. Some of the major barriers are the access to a device and the requirement of advanced training and experience [13].

US-guided insertion of central venous catheters is considered a common practice in developed countries; however, there is a lack of information about the patterns of using this technique in low- income countries. We sought to describe and analyse the current use of US guidance for insertion of central venous catheters by Colombian anaesthesiologists.

INITIAL ASSESSMENT AND IMPLEMENTATION

Approach

The Institutional Review Board and the Research Ethics Committee from the Colombian Society of Anaesthesiology and Resuscitation (SCARE, for the term in Spanish) approved this study. Inclusion of participants in this study required electronic acceptance, but the written consent was waived by the committee because of the low risk represented by this study and the strict confidentiality and anonymity strategies for data management.

Sampling and recruitment

This study involved anaesthesiologists and fellows in anaesthesia registered in the SCARE database. Inclusion criteria included being registered in the database and accepting to answer an electronic web-based survey sent via email. There were no exclusion criteria. Two people with prior training from the authors of the protocol at the Universidad del Cauca in Colombia conducted the questionnaire and collected the data without knowledge of the study objectives to avoid observer-expectancy bias.

Choice of solution

The survey contained 15 questions (Supplementary material). The variables were grouped by the following sections: demographic variables (age, gender and current academic degree) and clinical variables (anaesthesia expertise, years of anaesthesiology practice, US availability, use of US, reasons for not using US, training experience and complications). To assess the use of US guidance for the insertion of central venous catheters, we used a passive question to reduce the risk of bias (Do you use US guidance for insertion of central venous catheter?) and the answer options for that question were 'Always', 'Sometimes', 'Rarely' and 'Never'. For purposes of statistical analysis, we categorised this variable in 'Use of ultrasound' that included the options Always/Sometimes and 'Do not use ultrasound' included Rarely/Never. The first option was used as the main outcome under study. Specialised personnel from the SCARE designed the interface of the electronic web-based survey. The format and answer options were carefully revised and all authors discussed the questions before delivering such via email to the study population.

Data analysis

The time interval between delivering the survey and closing the option for input was 2 months. First, an initial exploratory analysis of the respondents was performed by describing the quantitative variables in averages with their respective standard deviations (SD) or median with interquartile ranges (IQR) according to the normal data distribution. Qualitative variables were expressed with absolute values as frequencies or proportions, with their respective 95% confidence interval (95% CI). Thereafter, a univariate analysis was per- formed, comparing the variables in order to use (grouping the options 'Always' and 'Sometimes') or not use (grouping the options 'Rarely' and 'Never') US for CVC. Comparison of qualitative variables was performed by using chi-squared test ($\chi 2$) and Student's t-test. We con- ducted a logistic regression for the multivariate analysis by using a model that includes age, gender and professional degree. We calculated the linear trend for the relation of age versus percentage of US users. We considered a P-value <0.05 as statistically significant. The data was analysed in the R statistical software [14].

EVALUATION

Participants

From July to September 2016, 351 responses were collected, which resulted in a response rate of 12.3% (351/2850). The respondents were predominantly general anaesthesiologists 76% (n=266), followed by other fellowships, such as cardiovascular anaesthesia 9% (n = 30), intensive care 6% (n = 20), neuro-anaesthesia 3% (n = 10), paediatric anaesthesia 2% (n = 7), obstetric anaesthesia 1% (n = 4) and other sub-specialisations 4% (n = 14). The mean age of the respondents was 44 years (SD = 9.9 years) and the male:female ratio was 3.2:1.

Use of US guidance during CVC insertion

The proportion of respondents who reported using US sometimes and always for guidance during CVC was 45% (95% CI 39–50%) (n = 157). Table 1 shows the characteristics of the US-guided CVC by Colombian anaesthesiologists.

Colombian anaesthesiologists (n = 157).

The participants with US equipment available 'all the time' in their workplaces were 62.7% (n = 220). The main reason given for not using or only having limited use of US guidance for CVC was the lack of US equipment in 50% of cases (n = 174) while a minority admitted that the use of US exceeds their clinical abilities 5% (n = 18). The training on this technique was variable, 50.4% (n = 177) of the respondents have had external courses, 22.8% (n = 80) have acquired experience from colleagues, 29.3% (n = 103) from empirical experience and 16% (n = 56) have never received training on this technique.

Determinants of the use of US guidance

Univariate analysis showed that age (<40 years) and availability of US were related with the use of US for CVC. Figure 1 illustrates the linear trend of the use of US depending on age ($P < 0.001$). After adjusting for covariates (gender and professional degree) availability of US was an independent factor associated with use of the technique. Table 2 shows details of the univariate and multivariate analyses.

LESSONS LEARNED

This study describes the current patterns of using US for CVC among Colombian anaesthesiologists. Our results demonstrated that US guidance is not a common practice for CVC and it appears that availability of this technology is an important limitation to its use.

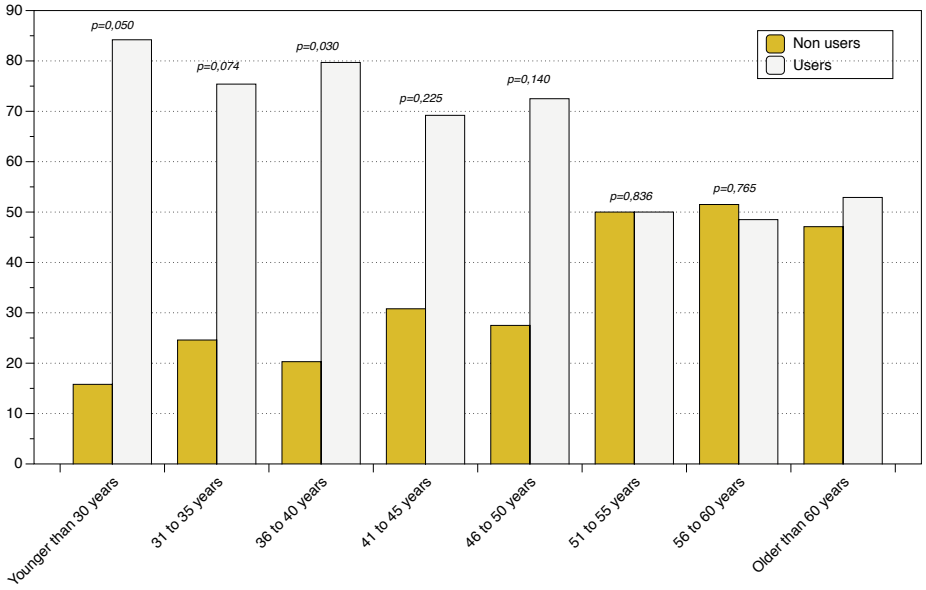

Figure 1. Relationship between age and proportion of US use during CVC (n = 351).

Table 1. Characteristics of the US-guided technique for CVC by Colombian anaesthesiologists (n = 157).

Characteristic	n (%)
Time of US guidance	
Since the beginning of the procedure	153 (97%)
When there are difficulties of insertion	4 (3%)
Technique used	
Real-time US-guided insertion	156 (99%)
Anatomic assessment without guidance	1 (1%)
Needle approach	
In plane	76 (48%)
Out of plane	81 (52%)

Abbreviations, US: ultrasound, CVC: central venous catheterization.

The prevalence of US guidance for CVC by Colombian anaesthesiologists was 45%. The range of proportions reported in the literature varies between 15% and 96% [13, 15–20], depending on the population, year of the survey [16], country and other settings.

Table 3 describes studies that have assessed the use of US for CVC. Note a high qualitative heterogeneity among studies clearly reflected in the different rates of US use. Our results show that Colombian anaesthesiologists, compared with other scenarios from high-income countries, underuse US.

Table 2. Univariate and multivariate analyses for the relation between covariates and the use of US guidance during CVC (n = 351)

Variable	Univariate analysis		Multivariate analysis	
	OR	P value	Adjusted OR [95% CI]	P value
Age [years]				
≥ 61	Ref.		Ref.	
56 – 60	0.83	0.77	0.61 [0.11 – 3.30]	0.57
51 – 55	0.88	0.84	0.33 [0.06 – 1.62]	0.17
46 – 50	2.34	0.14	2.50 [0.51 – 12.1]	0.26
41 – 45	2.00	0.23	1.72 [0.35 – 8.32]	0.50
36 – 40	3.48	0.03	2.78 [0.58 – 13.2]	0.20
31 – 35	2.71	0.07	2.77 [0.58 – 13.1]	0.20
≤ 30	4.74	0.05	3.11 [0.38 – 25.3]	0.29
Gender				
Male	Ref.		Ref.	
Female	2.14	0.01	1.29 [0.55 – 3.05]	0.55
Type of anaesthesia practice				
General	Ref.		Ref.	
Cardiovascular	2.64	0.06	2.78 [0.79 – 9.77]	0.11
Intensive care	1.20	0.68	1.99 [0.56 – 7.02]	0.28
Neuro-anaesthesia	2.10	0.35	1.45 [0.14 – 15.2]	0.75
Other	1.60	0.29	0.76 [0.16 – 3.49]	0.73
Technology availability				
Not available	Ref.		Ref.	
Available	27.4	< 0.001	38.6 [18.5 – 80.3]	< 0.001

$R^2 = 0.57$

To our best knowledge, sufficient evidence is unavailable about US use for CVC in developing countries. Despite the potential of US-based imaging to improve the diagnosis of many medical conditions and to guide individual patient management, we know little about current practices in low- and middle-income countries, such as the extent of use of portable US devices, major indications for the use of US techniques and impact on patient outcome. A recent systematic review did not find any study on the use of US during CVC [22]. Most current applications focus on obstetrical and abdominal complaints, with a lack of high-quality evidence from developing countries [22]. In terms of procedural US in the developing world, most evidence relates to peripheral venous access, ultrasound-guided thoracentesis or paracentesis and regional anaesthesia [23].

A well-documented association exists between availability of US equipment and use of this technique for CVC [11, 20]. Our survey reports conflictive results in terms of using US in operating rooms. Although 62% of the participants report having US equipment

Table 3. Similar survey studies about use of US guidance during CVC insertion in other scenarios around the world

Study	Country	Participants	Percentage of US-guided CVC	Comments
Adhikari et al. 2015.[16]	USA	Emergency medicine residents	53%, 96%	Increasing of ultrasound use from 2007 to 2013.
Bailey et al. 2007.[13]	USA	Members of the Society of Cardiovascular Anaesthesiologists	15% (223/1494)	Availability of US equipment was associated with use of US (OR=18.9, P<0.001).
Bosman et al. 2006.[15]	UK	Paediatric anaesthesiologists	68% (133/196)	-
Girard et al. 2005.[17]	USA	Surgery, anaesthesia, emergency medicine, internal medicine and family medicine house staff	15% (19/137)	A total of 19 anaesthesiologists were surveyed, of which only 5 use US with a frequency of 21%-60%.
Lindgren et al. 2013.[18]	Sweden	Anaesthesiology and intensive care departments	53% (26/49)	-
Schummer et al. 2007.[19]	Germany	Anaesthesia departments	40% (188/468)	12.7% routinely and 60% when faced difficulties
Soni et al. 2016.[20]	USA	Intensivist and Hospitalist	82.5% (647/784)	US guidance varied by site from 80% for internal jugular vein to 31% in subclavian vein.
Tovey et al. 2006.[34]	UK	Paediatric anaesthesiologists	49% (104/212)	-

inside the operating room, they also report the absence of equipment as a reason for not using it. Many hospitals in Colombia only have a single portable US device for use in many services and wards. Therefore, knowing that the equipment is available at the hospital does not guarantee its use all the time; this could explain the difference between availability and actual usage during CVC.

Access to US has increased significantly in resource-limited settings, including the developing world. A survey on perceived barriers in the use of US in low- and middle-income settings identified lack of training as a primary barrier to regular use of US in their practice, followed by lack of equipment. Equipment requirements, including maintenance and cost of machines, are also important factors [24]. Our results show availability of equipment as an independent factor for using the technique among respondents, but this potential association should be taken with caution due to the very high uncertainty with the broad CI of the estimation.

The World Bank currently identifies Colombia as a middle- income country, but it is still in the process of developing a modern healthcare and academic system. Most anaesthesiology residency programs in Colombia have begun to incorporate US into their education, training, and clinical practice to improve the quality and safety of healthcare.

However, even in some of Colombia's most advanced urban university-based hospitals, limited resources are still a reality. In addition, there is a lack of evidence related with the current use of procedural US. Henwood et al. [25] conducted a nationwide survey of Colombian emergency medicine residents designed to explore the state of US use and examine barriers for its expansion. The most frequently indicated barriers to ultrasound use were lack of instructors, equipment and time. We consider this finding could also be valid for anaesthesiologists and other specialisations.

Patient safety is a priority in this revolutionary era of technology [26, 27]; catheterisations have inherent risks of mechanical, infectious and haemodynamic complications [16]. Mechanical complications (e.g. arterial puncture, failure rates of insertion, haemothorax and pneumothorax) are common and independently increased by the number of attempts [28]. A recent Cochrane systematic review compared US guidance versus a landmark technique for CVC and concluded that US guidance is significantly associated with lower number of attempts needed for successful catheterisation, increased chances of success at the first attempt, and reduced possibilities of haematoma formation. However, this technique did not show a significant reduction in mechanical complications, such as arterial punctures or time for successful catheterisation [6].

The infectious risk of US equipment is a controversial concern of this technique. This concern is based on a recent outbreak in which sterile gel acted as a vehicle for the spread of infection to patients. This led to a product safety alert by the United States Food and Drug Administration [29]. However, a recent prospective observational study rejected this hypothetical association [30].

In this study, age seems to be related to not using US guidance during CVC. We found a non-adjusted linear trend depending on the age of the anaesthesiologist, which disappeared after multivariate analysis. Regarding this finding, there is growing evidence on the effect of age on practitioners' performance. Aging is associated with decreased processing speed, limiting ability to complete complex tasks, increased difficulty for information processing, reduced hearing and visual acuity, and decreased manual dexterity and visuo- spatial ability [31–34]. US guidance requires motor and visuospatial skills that aging practitioners may have not acquired or have lost. In addition, young anaesthesiologists could have greater exposure to US training during their residency programmes. On the other hand, older practitioners may feel they have developed enough experience allowing them to perform the insertion without the US technique.

Study limitations

This study had important limitations, including a small sample size. We used the database of all anaesthesiologists registered in SCARE (~2850) although many of them are not active practitioners. The response rate can be considered acceptable, compared with other similar online-based surveys. Additionally, the respondents using US guidance could be

more motivated to complete the questionnaire in which case the frequency of use of US for CVC in this study would be overestimated. Another limitation is the study design in which the accuracy and self-reporting information from participants was assumed correct because direct observations were not conducted. All the questions included in our survey were closed ended, which might have introduced response bias. Finally, the questions used in the questionnaire did not distinguish the use of US for internal jugular, subclavian, or femoral vein catheterisation.

CONCLUSION

Use of US for CVC is not a common practice among Colombian anaesthesiologists. Limited availability of this technology in healthcare centres hinders the use of this technique. Only half of the respondents have taken an external course to learn about US Management, the rest admitted to acquiring experience by themselves or from colleagues. More education and strict compliance of protocols on this technology would be helpful for safer CVC. Further, US guidance can be used in many other procedural applications, like regional anaesthesia, basic echocardiography, vascular assessment, pleural drainage, pulmonary US, and others, ensuring safety and quality of care.

APPENDIX

ULTRASOUND GUIDANCE FOR CENTRAL VENOUS CATHETERISATION. A COLOMBIAN NATIONAL WEB-BASED SURVEY

How old are you?
Answer:

Gender:
Male
Female

Which year did you graduate from residency?
Answer:

Which specialty do you practice?
General:
Cardiovascular:
Paediatric:
Intensive care:
Neuroanaesthesia:
Other:

Is ultrasound equipment available in your workplace?
Yes:
No:

Do you use ultrasound-guidance during insertion of central venous catheter?
Always:
Often:
Rarely:
Never:

What is the reason for not using ultrasound-guidance for insertion of central venous catheter?
It is not needed:
It increases costs:
It is time consuming:
It is not available:

It decreases the ability for insertion of CVC:
I always use ultrasound:

How was your training on ultrasound?
External courses:
Colleagues:
Experience:
None:

Do you think that ultrasound is important for guidance during the insertion of central venous catheter?
Yes:
No:
Sometimes:

In which cases do you use ultrasound-guidance?
Since the beginning of the procedure:
Only when I have difficulties:

What is the utility of ultrasound during insertion of CVC?
For real-time guidance:
For looking at the anatomy before insertion:

What approach do you usually use for ultrasound-guidance?
In plane:
Out of place:

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Chapter 4

Incidence of Mechanical Complications of Central Venous Catheterization Using Landmark Technique: Do Not Try More Than 3 Times.

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ABSTRACT

Purpose

Central venous catheterization is a standard procedure in intensive care therapy. In developing countries, this intervention is frequently performed by physicians in training and without the availability of ultrasound guidance. Purpose of this study was to determine the incidence and potential risk factors for mechanical complications during central venous catheterization in an intensive care setting performed by a mixed group of practitioners without the use of adjunct ultrasound.

Methods

Prospective observational cohort study in a university teaching hospital. Three hundred critically ill patients requiring their first central venous catheter insertion were enrolled. All patients were observed for 24 hours for mechanical complications (pneumothorax, hemothorax, arterial puncture, incorrect tip position, cardiac dysrhythmia, and/or subcutaneous hematoma). Potential associations with mechanical complications were adjusted using multivariable analysis. Main outcome was the cumulative incidence of mechanical complications.

Results

The incidence of mechanical complications was 17% (n = 51). After covariate adjustment, the number of punctures was significantly related to mechanical complications. Compared with 1 puncture, 3 or more attempts were significantly associated with mechanical complications (odds ratio 3.62 [95% confidence interval 1.34-9.8]; $P = .011$). Experience of the operator was not associated with mechanical complications.

Conclusions

The incidence of mechanical complications is affected by the number of punctures performed. After adjustment, the risk increases substantially with more than 3 attempts. Limiting the number of attempts, appropriate supervision and the use of ultrasound guidance when available are recommended for the further reduction in mechanical complications of central venous catheterization.

Keywords

catheterization, central venous, mechanical complications, central venous catheter

INTRODUCTION

Central venous catheters (CVCs) are widely used in critically ill patients in intensive care units (ICUs). Several studies report a high prevalence of use ranging from 32% up to 80%.(1,2)

Central venous catheters are used for monitoring hemodynamic variables, for delivering medications, intravenous fluids, parenteral nutrition, or hemodialysis. However, some mechanical complications have been well described (3-5) including failure to place the catheter, incorrect tip position, pneumothorax, hemothorax, arterial puncture, dysrhythmia, and death. These complications are reported to have an incidence from 5% to 34%. (4,5)

To categorize factors related to mechanical complications, Polderman and Girbes divided those in 4 main categories: catheter-related factors, patient-related factors, site-related factors, and use- and care-related factors. (3) Risk factors for mechanical complications are well described, such as subclavian versus other sites, female gender, advanced age, extremes of body mass index (BMI), prior catheterization, surgery or radiotherapy, number of punctures, time needed to placement, and experience of the operator. (4,6-9) Nevertheless, some factors such as operator's experience show conflicting evidence. (6,8,10-12)

We aimed to study the incidence of mechanical complications of central venous catheterization in a single-center, university-affiliated ICU in Popayan, Colombia, placed by physicians with varying levels of experience and training. In addition, we identify factors related to their occurrence, and we compared our results to published data worldwide adding evidence from developing countries.

METHODS

We collected data of all patients older than 18 years of age undergoing CVC insertion from January to July 2008. This study was conducted after approval of ethics committee board in a 20-bed medical and surgical ICU in La Estancia Clinic, Popayan, Colombia, a 300-bed university-affiliated urban hospital.

Demographic and anthropometric variables, main diagnosis of admission, comorbidities, indication for CVC placement, and information related to insertion procedure were recorded. The choice of catheter site was at the discretion of the operator.

All catheters were placed in the jugular (internal or external) or subclavian vein by (1) house medical intensivist or specialist staff (experienced attendant), (2) residents in anesthesiology, internal medicine, and surgery (medical residents in training with less than 3 years of experience at intensive care setting), or (3) general practitioners (medical

house doctors without specialization). Residents and general practitioners placed the catheters always under direct supervision of 1 staff member of group 1.

Insertion was performed as a complete sterile procedure in all cases. All catheters were inserted using the standard Seldinger landmark technique. Devices used were triple-lumen, double-lumen, or single-lumen catheters (Multi-Med Central Venous Catheter Kit; Edwards Lifesciences LLC, Irvine, California).

All attempts and punctures (in order) to position the catheter were counted independent of the finally selected site. Each of those punctures can potentially increase the risk of mechanical complications. Once the catheter was inserted, it was sutured and covered with sterile drape. Catheter position was con- firmed by free fluid flow through all lumens and hemodynamic waveform visualization. Immediately after, an x-ray control was made for all patients.

All patients were observed for presence of mechanical complications during a period of 24 hours after the procedure. Our main outcome was the cumulative incidence of mechanical complications, defined as the occurrence of 1 or more of the following events: incorrect tip position (catheter's tip not in superior vena cava with less than 40º of angle between the vessel wall and the catheter tip) (13) confirmed by the x-ray control, pneumothorax, hemothorax, arterial puncture, cardiac dysrhythmia, and subcutaneous hematoma (any evidence of skin hematoma at the [intended] insertion points).

Patient characteristics recorded were age, gender, BMI, Acute Physiology and Chronic Health Evaluation II score at ICU admission, main diagnosis at admission (medical vs surgical or postoperative), prior use of CVC, presence of mechanical ventilation during the procedure, and main indication for placement of the CVC. Procedure characteristics were site of insertion, number of total punctures performed, time during the procedure (day [7 AM to 7 PM] vs night), type of catheter used (trilumen/bilumen/others), and training level of the operator.

Data Analysis

We described continuous variables as means + standard deviations and categorical data frequencies and percentages. Data nonnormally distributed were reported as median and range.

We performed bivariate unadjusted comparison of the catheter insertion site with the presence of mechanical complications as composite end point and with each compound, as well. A significance level of $P < .05$ was considered statistically significant. Independent variables were analyzed in a bivariate way with mechanical complications using the chi-square test or t test for independent samples, as appropriate. In addition, this analysis was done with exclusion of minor complications (subcutaneous hematoma and incorrect tip position).

Potential associations with mechanical complications were adjusted with a multivariate approach. We fitted a logistic regression model with the following continuous and

categorical predictors: BMI and number of punctures, main diagnosis at admission (reference category [rc]: surgical, 1: medical), mechanical ventilation (rc: absent, 1: present), time during the procedure (rc: day, 1: night), place of CVC (rc: external jugular, 1: internal jugular, 2: subclavian), and training level of the operator (rc: intensivist/specialist, 1: resident, and 2: general practitioner as defined in methods section).

To explore the effect of several punctures versus 1, we constructed a second logistic regression model introducing this as a categorical parameter. To assess the correlation between the number of punctures and the level of training of the operator, a Poisson regression was done using "number of punctures" as outcome and "level of training" as predictor.

Analysis was done in SPSS 17 (SPSS Statistics for Windows, Version 17.0; SPSS Inc, Chicago). All regression models were made using enter method. We presented our results in terms of odds ratios (ORs) and 95% confidence intervals (95% CIs). Possible effect modifications were tested. Hosmer and Lemeshow statistic test was used to test goodness of fit in selected models. To investigate the lack of fit in models, we carried out residual analysis.

RESULTS

We collected 300 consecutive patients who required CVC insertion on the ICU. General characteristics of the patients and the procedure are presented in Table 1. In most patients, a medical diagnosis was the cause of ICU admission, and the main indication to insert a catheter was hemodynamic monitoring or drugs/fluids infusion. There were 218 (72.6%) subclavian attempts and half (51%) of all catheters were placed by residents. The proportion of catheters successfully inserted at the first attempt was 86.7%.

Mechanical complications in relation to insertion place are described in Table 2. Fifty-one patients presented 1 or more mechanical complications. The incidence of mechanical com- plications was 17%. In all, 40 (13.3%) patients required a change in the initial site of puncture, and there were no patients with failure to place a CVC. In all, 16 (5.3%) patients presented major mechanical complications (arterial puncture, pneumothorax, and/or hemothorax).

Bivariate analysis showed significant associations with the presence of total mechanical complications for medical diagnosis at intensive care admission ($P = .013$) and mechanical ventilation during the procedure ($P = .01$). After adjustment for covariates, only the number of punctures showed a significant association (as continuous variable) with mechanical complications (OR 1.87 [95% CI 1.47-2.38]; $P = .000$; Table 3). Compared with 1 puncture, 3 or more attempts were significantly associated with mechanical complications (OR 3.62 [95% CI 1.34-9.8]; $P = .011$; Table 4 and Figure 1). There was no association between the number of punctures needed and the level of training of the operator ($P = .114$).

Table 1. General Patients and Procedure Characteristics of the Population. [a]

Patient's characteristics	
Male gender[b]	148 (49%)
Age, years[c]	60 ± 19
BMI,[c] kg/m^2	23.7 ± 4.3
APACHE II scored	15 (10-20)
Main diagnosis (medical/surgical)[b]	254 (85%) / 46 (15%)
Prior use of central venous catheter[b,e]	53 (18%)
Mechanical ventilation[b]	225 (75%)
Main indication to use central venous catheter[b]	
Hemodynamic monitoring	244 (81%)
Vasopressor infusion	234 (78%)
Infusion of special drugs	139 (46%)
Venous pacemaker use	11 (4%)
Hemodialysis access	10 (3%)
Swan-Ganz catheter insertion	7 (2%)
Insertion site of central venous catheter[b]	
Right subclavian	171 (57%)
Left subclavian	47 (15.7%)
Right internal jugular	47 (15.7%)
Right external jugular	18 (6%)
Left internal jugular	12 (4%)
Left external jugular	5 (1.6%)
Insertion characteristics	
Catheters successfully inserted at the first attempt[b]	260 (86.7%)
Number of punctures[c,d]	1.8 ± 1.3, 1 (1-9)
Trilumen catheter use[b]	259 (86%)
Insertion during the day (7 AM - 7 PM)[b]	187 (62%)
Training level of the operator[b]	
General practitioner	70 (23%)
Resident in training	153 (51%)
Intensivist/specialist (attendant)	77 (26%)

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; BMI, body mass index; CVC, central venous catheter; ICU, intensive care unit; SD, standard deviation.

[a]n=300.

[b]Data presented as number and percentage (%).

[c]Data presented as mean ± SD.

[d]Data presented as median and (range).

[e]Refers to the patients who used a CVC during a prior hospitalization or ICU stay.

Table 2. Total and Major Mechanical Complications and Site of Insertion of Central Venous Catheters.

	Total (n=300)	Subclavian (n=218)[a]	Internal Jugular (n=59)[a]	External Jugular (n=23)[a]	*P*
Mechanical complications[b]	51 (17)	39 (17.9)	11 (18.6)	1 (4.3)	0.154
Arterial puncture	13 (4.3)	8 (3.6)	5 (8.4)	0	0.122
Pneumothorax	2 (0.6)	2 (0.9)	0	0	0.527
Hemothorax	1 (0.3)	1 (0.45)	0	0	0.726
Incorrect tip position	13 (4.3)	13 (5.9)	0	0	0.014
Subcutaneous hematoma	31 (10.3)	21 (9.6)	9 (15.2)	1 (4.3)	0.273

[a]There were no significant differences between right and left positions at each site.
[b]Data presented as number and percentage (%) of the total catheters inserted at each site. 95% confidence limits for incidence proportion (12.7%-21.2%).

Table 3. Multivariate Analysis.[a]

	Model Number I[b]	
	Adjusted OR (95% CI)	*P*
BMI, kg/m2	0.9 (0.92-1.07)	ns
Medical diagnosis at admission	3.9 (0.88-17.9)	ns
Under mechanical ventilation	0.61 (0.29-1.26)	ns
Insertion during the day	1.04 (0.51-2.13)	ns
Site of CVC (rc: external jugular)		
Internal jugular	1.6 (0.1-15)	ns
Subclavian	3.1 (0.3-26)	ns
Operator (rc: intensivist/specialist)		
Resident	1.42 (0.56-3.5)	ns
General practitioner	1.1 (0.38-3.5)	ns
Number of punctures	1.87 (1.47-2.38)	0.000

Abbreviations: BMI, body mass index; CI, confidence interval; CVC, central venous catheter; OR, odds ratio; NS, not significant; rc, reference category.
[a]Logistic regression model 1.
Outcome under study: presence of mechanical complications as continuous outcome.
[b]Hosmer and Lemeshow test P = .98.

Table 4. Multivariate Analysis.[a]

		Model Number 2[b]	
	n (%)	Adjusted OR (95% CI)	*P*
Number of punctures (rc: 1 puncture)	184 (61)	n/a	n/a
Two punctures	59 (20)	1.36 (0.53-3.45)	ns
Three punctures	27 (9)	3.62 (1.34-9.8)	0.011
Four punctures	13 (4)	6.8 (1.9-24.2)	0.003
Five or more punctures	17 (6)	26.4 (7.2-96.6)	0.000

Abbreviations: n/a, not applicable; ns, not significant; OR, odds ratio; rc, reference category.
[a]Logistic regression model 2. Categorical analysis of number of punctures.
[b]Hosmer and Lemeshow test P = .62.

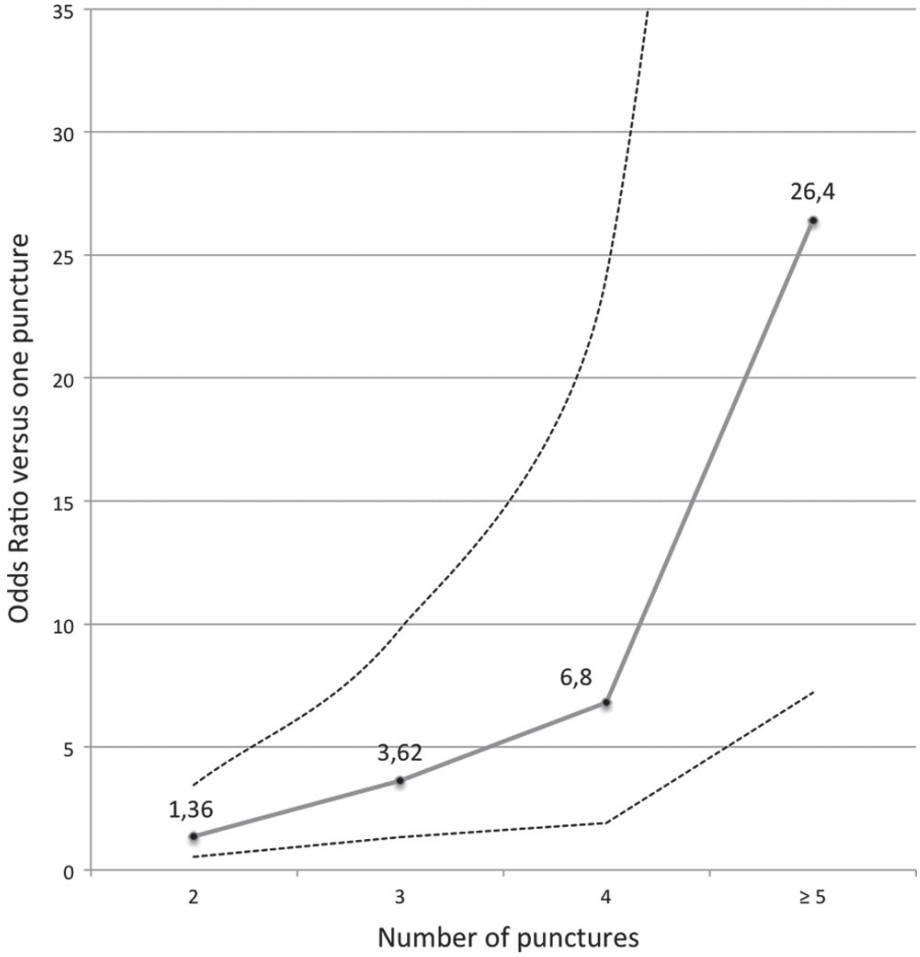

Figure 1. Increase in mechanical complication odds ratio with number of punctures. Dotted lines represent 95% confidence interval around odds ratio (OR).

DISCUSSION

This study confirms the strong relationship between number of punctures and incidence of mechanical complications during central venous catheterization. After adjustment for covariates, only the number of punctures remained significantly associated with mechanical complications. The increase in the odds ratio with each of the following puncture compared with the previous one is 1.9. Mansfield et al described how the rate of complications increases with more than 2 passes of the needle. (6) Later on, Eisen et al showed an odds ratio of 3.6 with more than 2 punctures. (4) Our findings are consistent with these previous studies and confirm the importance of the number of punctures and mechanical complications during central venous catheterization. Additionally, we are

able to demonstrate that the increased odds ratio with more punctures in comparison with one has a linear slope until 3 punctures after which the curve becomes exponential. Our results support the recommendation not to perform more than 3 punctures at the same site. After that a central catheterization should be attempted at another site.

Currently, there is no clear, precise, and widely accepted definition for mechanical complication of central venous catheterization. This affects the incidences reported in different studies. In fact, in our study, we found an incidence of 17% of mechanical complications. If we exclude minor complications (such as subcutaneous hematoma), this incidence is reduced to 9.3% (n = 28). These results are in accordance with worldwide data reported previously. (4,5,8,14-17)

Studies report mechanical complications as combined end points; however, each complication can be produced and explained by different processes. Merrer et al counts major mechanical complications only if they require a specific therapeutic intervention, otherwise it was classified as minor. (15) Many authors do not explicitly classify mechanical complications as major or minor and describe details of each event. (6-9, 12,16) The most frequent complication we found in our cohort was a sub-cutaneous hematoma. This finding is not consistent with other studies and may represents the difficulties in defining and assessing the presence of a subcutaneous hematoma. (4) Fortunately, most authors agree that it is a minor complication and usually recovers spontaneously.

Arterial puncture was a frequent complication in our study, occurring in 4% of all patients. Some studies report incidences of arterial puncture from 0.9% to 10.6%, (12,18) but most of them are around 4%. (4-6,15,19)

The external jugular vein drains into the subclavian vein lateral to the junction of the subclavian vein and the internal jugular vein. It is used for central venous catheterization, with and without ultrasound. (11,20,21) Although the external jugular vein is one of the most easily detectable and accessible vessels in the neck, it has not been considered the first choice for central venous catheterization, as there is a relatively high failure rate in catheter placement. (22,23) Variations at the termination point and angulation of the external jugular vein as it enters the subclavian vein contribute to this failure rate. However, some experienced authors show a high rate of catheterization success, reported from 50% to 90%. In addition, this approach carries fewer risks of major complications. (21,23) In our clinical practice, we use this site when the patient appears to present difficulties for other approaches or when other approaches fail. In fact, in our study, we did not have any failure of positioning 23 external jugular catheters.

Half of the catheterizations were performed by residents in training. The experience of the operator could be related to the number of attempts performed; nevertheless, our data do not support this statement, and after adjustment, there was no significant association between the number of punctures and the presence of mechanical complications. Likewise, other authors have not showed this relationship. (4,8) In our center,

residents and general practitioners even in early stages of their training have to perform numerous invasive interventions in ICU patients and on the operating room. Currently, there is no formal standardized training, for example, with a simulator, but in all cases, they perform these interventions under direct supervision of an experienced senior staff member.

We did not find any relationship of age, gender, BMI, time of the day, and experience of the operator with the incidence of mechanical complications. These findings are in agreement with results reported by Eisen et al. (4) On the other hand, some methodological limitations could introduce a potential bias in this study such as underreport of complications (ie, subcutaneous hematoma) or subjective evaluation of the outcomes.

The use of ultrasound imaging for central venous cannulation greatly improves first-pass success and reduces complications. (24) In addition, cost-effectiveness analyses of ultrasound guidance have been shown to reduce human and economic resources. (25,26) Therefore, practice recommendations for the use of this technology have emerged from several sources (27-29) and currently ultrasound guidance should be used when available. Unfortunately, the availability of ultrasound training and imaging at the patient's bedside is not widely accessible in developing countries. Therefore, our study not only reflects some technological and health care limitations but also presents a potential area of improvement. Currently, our hospital has included the use of ultrasound guidance as part of the quality of care program.

However, using landmark technique, our results present interesting parallels with other, well-developed areas around the world. In conclusion, the incidence of mechanical complications with central venous catheterization in our center is 15% and is mostly affected by the number of punctures performed but not related to the experience of the operator. The risk increases substantially when more than 3 attempts are made. Therefore, based on the current knowledge, appropriate supervision and the use of ultrasound guidance when available are always recommended.

DECLARATION OF CONFLICTING INTERESTS

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Chapter 5

Anaesthesia for evacuation of incomplete miscarriage. Cochrane Systematic Review.

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ABSTRACT

Background

An incomplete miscarriage occurs when all the products of conception are not expelled through the cervix. Curettage or vacuum aspiration have been used to remove retained tissues. The anaesthetic techniques used to facilitate this procedure have not been systematically evaluated in order to determine which provide better outcomes to the patients.

Objectives

To assess the effects of general anaesthesia, sedation or analgesia, regional or paracervical block anaesthetic techniques, or differing regimens of these, for surgical evacuation of incomplete miscarriage.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (23 January 2012), CENTRAL (*The Cochrane Library* 2012, Issue 1), PubMed (1966 to 23 January 2012), EMBASE (1974 to 23 January 2012), CINAHL (1982 to 23 January 2012), LILACS (1982 to 23 January 2012) and reference lists of retrieved studies.

Selection criteria

All published and unpublished randomised controlled trials (RCTs) or cluster-RCTs comparing the use of any anaesthetic technique (defined by authors as general anaesthesia, sedation/analgesia, regional or paracervical local block (PCB) procedures) to perform surgical evacuation of an incomplete miscarriage. We excluded quasi-randomised trials and studies that were only available as abstracts.

Data collection and analysis

Two review authors independently assessed studies for inclusion and assessed risk of bias. Data were independently extracted and checked for accuracy.

Main results

We included seven trials involving 800 women. The comparisons revealed a very high clinical heterogeneity. As a result of the heterogeneity in the randomisation unit, we did not combine trials but reported the individual trial results in the 'Data and analysis' section and in the text. Half of trials have unclear or high risk of bias in several domains.

We did not find any trial reporting data about maternal mortality. In terms of postoperative pain, PCB does not improve the control of postoperative pain when it is compared against sedation/analgesia or versus no anaesthesia/no analgesia. In the comparison of

PCB with lidocaine versus PCB with saline solution, significant differences favouring the group with lidocaine were found in one trial (moderate or severe postoperative pain) (risk ratio (RR) 0.32; 95% confidence interval (CI) 0.18 to 0.59).

When opioids were used, postoperative nausea and vomiting was more frequent in two trials comparing those versus PCB. In terms of requirement of blood transfusion, two trials showed conflicting results.

Authors' conclusions

Particular considerations that influence the choice of anaesthesia for this procedure such as availability, effectiveness, safety, side effects, practitioner's choice, costs and woman's preferences of each technique should continue to be used until more evidence supporting the use of one technique or another.

Keywords

Abortion, Incomplete [*surgery]; Anesthesia, General [*methods]; Anesthesia, Obstetrical [*methods]; Dilatation and Curettage [adverse effects, *methods]; Female; Humans; Hypnotics and Sedatives [therapeutic use]; Pain, Postoperative [*prevention & control]; Patient Satisfaction; Postoperative Nausea and Vomiting [etiology]; Pregnancy

BACKGROUND

Description of the condition

Miscarriage is when a pregnant woman loses her baby before the baby would be considered able to survive outside the womb, i.e. before 24 weeks' gestation. Miscarriage occurs in about 10% to 15% of pregnancies and the clinical signs are bleeding, usually with some abdominal pain and cramping (Shiers 2003).

An incomplete miscarriage occurs when all the products of conception are not expelled through the cervix (Bottomley 2009). After a clinical assessment suggesting complete miscarriage, 45% of women will have retained tissue on ultrasound (Alcazar 1995). Approximately 85% of incomplete miscarriages occur before the 12th week of pregnancy.

Traditionally, surgery (curettage or vacuum aspiration) has been the treatment used to remove any retained tissue and it is quick to perform. Nowadays, medical treatment is also available (Neilson 2010). This review is focused on anaesthesia used for surgical management.

Description of the intervention

Data from elective surgical abortions suggest that a major complication occurs in fewer than one in 100 women and mortality is around 0.7 in 100,000 (Bartlett 2004; Koonin 2000). Although the case-fatality-rate has decreased, anaesthesia-related events continue to be the leading cause of morbidity during the procedure (Lawson 1994).

To perform a surgical evacuation of incomplete miscarriage many anaesthetic techniques are used, including general anaesthesia, sedation/analgesia, regional and paracervical local block (PCB) anaesthesia. Key factors that influence the choice of anaesthesia include availability, effectiveness, safety, side effects, and costs. Other factors include woman preference, practitioner choice, facility resources and medical indications (Paul 1999).

How the intervention might work.

General anaesthesia and sedation/analgesia.

As defined by the American Society of Anesthesiologists, sedation/analgesia differ from anaesthesia because general anaesthesia is a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation. The ability to independently maintain ventilatory function is often impaired. Patients often require assistance in maintaining a permeable airway, and positive pressure ventilation may be required because of depressed spontaneous ventilation. In this situation, drug-induced depression of neuromuscular function and cardiovascular alterations may be present (ASA 2004). General anaesthesia can be provided with inhalational halogen agents (e.g.

Sevofluorano), intravenous agents like thiopental or propofol or combinations of both and it can be supplemented or balanced with other intravenous agents such as opioids or benzodiazepines.

Sedation and analgesia comprise a continuum of states ranging from minimal sedation (anxiolysis) through general anaesthesia. It is difficult to establish an exact limit between them, but sedation/analgesia could be classified in accordance to ranges (minimal sedation, moderate sedation or conscious sedation and deep sedation/analgesia). Sedation/analgesia allows patients to tolerate unpleasant procedures by relieving anxiety, discomfort, or pain (ASA 2002). This is often used in combination with a local anaesthetic technique at the site of surgery. Oftentimes, sedation/analgesia can have fewer side effects than may occur with general anaesthesia.

General anaesthesia provides adequate operating conditions for cervical dilatation and uterine intervention. However, there are some situations when it is hazardous, for example, when the patient is in a poor medical condition. Observational studies have shown that general anaesthesia is associated with increased morbidity and mortality in the context of surgical evacuation compared with other techniques (Peterson 1981). Furthermore, it is associated with higher costs and use of personnel (Grimes 1979; Paul 1999; Raeder 1992). However, about 80% of procedures are performed under general anaesthesia currently (Grimes 1979; Osborn 1990; Peterson 1981; Soulat 2006).

Regional anaesthesia and PCB.

Several obstetric and gynaecologic procedures are currently performed under regional nerve block including cervical dilatation and uterine evacuation. PCB anaesthesia offers an alternative for cervical dilatation and uterine interventions. It is performed with injection of local anaesthetic around the cervix, at the 'three and nine o'clock' positions, anaesthetising the second to fourth sacral nerve roots as they pass through Frankenhauser's plexus at a depth of 2 to 4 mm (Piyamongkol 1998). The advantages of PCB compared to general anaesthesia are that it does not require general anaesthetic equipment nor personnel trained to administer general anaesthesia. The World Health Organization is seeking a reduction in the total number of surgical interventions performed under general anaesthesia, in favour of local anaesthesia (WHO 1978). However, PCB anaesthetic should be administered by trained staff and resuscitation facilities should be available.

This technique and regional anaesthesia can be provided with local anaesthetics drugs such as bupivacaine or lidocaine that differ by action onset, potency, duration and toxicity (Toledano 2009). Fatal complications (i.e. cardiac arrest) associated with local anaesthetic toxicity used for PCB are reported in the literature (Grimes 1976).

Other regional neuraxial techniques (spinal and epidural) are less used for short procedures. Some authors report the advantages of epidural anaesthesia, including

diminished psychological reaction and the possibility of performing surgical procedures without any additional anaesthesia (Grunstein 1976).

Paracervical local anaesthesia for cervical dilatation and uterine intervention was covered in another systematic Cochrane review (Tangsiriwatthana 2009). For this reason, we plan to include trials that use PCB anaesthesia in the context of incomplete miscarriage evacuation only.

Why it is important to do this review

Surgical evacuation of incomplete miscarriage is a frequent procedure. Renner reported that 46 million procedures are performed every year worldwide (Renner 2009).

Although the surgical evacuation of an incomplete miscarriage is a short anaesthetic procedure, it is not free of complications. The exposure to the anaesthetic procedure becomes a risk to the life of the patient. The mortality associated with general anaesthesia is 0.37/100,000 procedures, and the rate with local anaesthesia is estimated around 0.15/100,000. The use of general anaesthesia is associated with a two-fold to four-fold increased risk of death from abortion at less than or equal to 12 weeks' gestation (Peterson 1981).

Additionally, moderate to severe postoperative pain is reported and postoperative nausea and vomiting could be present. Many patients still find surgical evacuation extremely uncomfortable and it could affect maternal psychological status (Renner 2009).

Some observational studies show that some anaesthetic techniques could be better than others. Moreover, the different techniques currently used have not been evaluated through systematic methods and there is at present no consensus about the method or technique to provide better outcomes for women.

OBJECTIVES

To assess the effects of general anaesthesia, sedation or analgesia, regional or paracervical block anaesthetic techniques, or differing regimens of these, for surgical evacuation of incomplete miscarriage.

METHODS

Criteria for considering studies for this review

Types of studies. We considered all published and unpublished randomised controlled trials (RCTs) or cluster-RCTs without language restrictions that compared the use of anaesthetic techniques or drugs to perform surgical evacuation of an incomplete mis-

carriage for inclusion in the review. We excluded quasi-randomised trials. We did not include studies that were only available as abstracts.

Types of participants. Women with a diagnosis of incomplete miscarriage undergoing management by surgical evacuation performed with general, sedation/analgesia, regional or PCB anaesthesia.

Types of interventions. We considered trials if they compared any anaesthetic technique given preoperatively or intraoperatively (defined by authors as general anaesthesia, sedation/analgesia, regional or PCB procedures) to perform a surgical evacuation of incomplete miscarriage with another anaesthetic technique. We also included comparisons between different drugs, routes of administration, duration or timing of treatment if data were available. We did not include trials that compared systemic analgesia with non-steroidal analgesic drugs alone or cyclooxygenase (COX) inhibitors.

Types of outcome measures. Primary outcomes: (1) Women's satisfaction with procedure (as defined by the authors). (2) Pain during and/or after surgical evacuation of miscarriage, which was measured as categorical or continuous data (visual analogue scale, requirement for additional analgesia consumption (mg/kg). (3) Maternal mortality.

Secondary outcomes: (1) Adverse events (postoperative nausea and vomiting, blood loss, hypotension, postoperative sedation).

Search methods for identification of studies

Electronic searches. We contacted the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group's Trials Register (23 January 2012).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from: quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL); weekly searches of MEDLINE; weekly searches of EMBASE; handsearches of 30 journals and the proceedings of major conferences; weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

In addition, we searched CENTRAL (*The Cochrane Library* 2012, Issue 1), PubMed (1966 to 23 January 2012), EMBASE (1974 to 23 January 2012), CINAHL (1982 to 23 January 2012), LILACS (1982 to 23 January 2012) using the search strategies detailed in Appendix 1, Appendix 2, Appendix 3, Appendix 4 and Appendix 5.

Searching other resources. We searched the reference lists of relevant studies. We did not apply any language restrictions.

Data collection and analysis

Selection of studies. Two review authors, Andrés Calvache (AC) and Mario Delgado (MD), independently assessed for inclusion all the potential studies identified as a result of the search strategy. We resolved any disagreement through discussion or, if required, we consulted a referee.

Data extraction and management. We designed a form to extract data. For eligible studies, AC and MD extracted the data using the agreed form. We resolved discrepancies through discussion or, if required, we consulted a referee.

When information regarding any of the above was unclear, we attempted to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies. Two review authors (AC, MD) independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We resolved any disagreement by discussion or by involving another review author.

(1) Random sequence generation (checking for possible selection bias). We described for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups. We assessed the method as: low risk of bias (any truly random process, e.g. random number table; computer random number generator); high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number); unclear risk of bias.

(2) Allocation concealment (checking for possible selection bias). We described for each included study the method used to conceal allocation to interventions prior to assignment and assessed whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment. We assessed the methods as: low risk of bias (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes); high risk of bias (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth); unclear risk of bias.

(3) Blinding of participants, personnel and outcome assessors (checking for possible performance bias). We described for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered studies to be at low risk of bias if they were blinded, or if we judged that the lack of blinding would be unlikely to affect results. We assessed blinding separately for different outcomes or classes of outcomes. We assessed the methods as: low, high or unclear risk of bias for participants; low, high or unclear risk of bias for personnel; low, high or unclear risk of bias for outcome assessors.

(4) Incomplete outcome data (checking for possible attrition bias due to the amount, nature and handling of incomplete outcome data). We described for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported and the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or was supplied by the trial authors, we re-included missing data in the analyses which we undertook. We assessed methods as: low risk of bias (e.g. less than 20% missing data; missing outcome data balanced across groups); high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; 'as treated' analysis carried out with substantial departure of intervention received from that assigned at randomisation); unclear risk of bias.

(5) Selective reporting (checking for reporting bias). We described for each included study how we investigated the possibility of selective outcome reporting bias and what we found. We assessed the methods as: low risk of bias (where it was clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review have been reported); high risk of bias (where not all the study's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest were reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported); unclear risk of bias.

(6) Other bias (checking for bias due to problems not covered by (1) to (5) above). We described for each included study any important concerns we had about other possible sources of bias. We assessed whether each study was free of other problems that could put it at risk of bias: low risk of other bias; high risk of other bias; unclear whether there is risk of other bias.

(7) Overall risk of bias. We made explicit judgements about whether studies were at high risk of bias according to the criteria given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). With reference to (1) to (6) above, we assessed the likely magnitude and direction of the bias and whether we considered it is likely to impact on the findings. We explored the impact of the level of bias through undertaking sensitivity analyses.

Measures of treatment effect. Dichotomous data. For dichotomous data, we presented results as summary risk ratio with 95% confidence intervals. Continuous data. For continuous data, we used the mean difference if outcomes were measured in the same way between trials. We used the standardized mean difference to combine trials that measured the same outcome, but used different methods.

Unit of analysis issues. We included cluster-randomised trials in the analysis along with individually randomised trials. We adjusted their standard errors using the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* using an estimate of the intracluster correlation co-efficient (ICC derived from the trial (if possible), or from another source. If ICCs from other sources were used, we reported this and conducted sensitivity analyses to investigate the effect of variation in the ICC. If we identified both cluster-randomised trials and individually-randomised trials, we planned to synthesise the relevant information. We considered it reasonable to combine the results from both if there was little heterogeneity between the study designs and the interaction between the effect of the intervention and the choice of randomisation unit was considered to be unlikely. We also acknowledged heterogeneity in the randomisation unit and performed a separate meta-analysis.

Dealing with missing data. For included studies, we noted levels of attrition. We explored the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis. For all outcomes, we carried out analyses, as far as possible, on an intention-to-treat basis; i.e. we attempted to include all participants randomised to each group in the analyses. The denominator for each outcome in each trial was the number randomised minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity. We assessed statistical heterogeneity in each meta-analysis using the T^2, I^2 and Chi^2 statistics. We regarded heterogeneity as substantial if I^2 was greater than 30% and either T^2 was greater than zero, or there was a low P value (less than 0.10) in the Chi^2 test for heterogeneity.

Assessment of reporting biases. In future updates of this review, if there are 10 or more studies in a meta-analysis, we will investigate reporting biases (such as publication bias) using funnel plots. We will assess funnel plot asymmetry visually, and use formal tests for funnel plot asymmetry. For continuous outcomes, we will use the test proposed by Egger 1997, and for dichotomous outcomes, the test proposed by Harbord 2006. If we detect asymmetry in any of these tests or if it is suggested by a visual assessment, we will performed exploratory analyses to investigate it.

Data synthesis. We carried out statistical analysis using the Review Manager software (RevMan 2008). We did not combine data in this review. In future updates, we will use fixed-effect meta-analysis for combining data where it is reasonable to assume that studies are estimating the same underlying treatment effect: i.e. where trials are examining the same intervention, and the trials' populations and methods are judged sufficiently similar. If there is clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if substantial statistical heterogeneity is detected, we will use random-effects meta-analysis to produce an overall summary if an average treatment effect across trials is considered clinically meaningful. The random-effects summary will

be treated as the average range of possible treatment effects and we will discuss the clinical implications of treatment effects differing between trials. If the average treatment effect is not clinically meaningful we will not combine trials. If in future updates of this review we use random-effects analyses, the results will be presented as the average treatment effect with 95% confidence intervals, and the estimates of T^2 and I^2.

Subgroup analysis and investigation of heterogeneity. In future updates, if we identify substantial heterogeneity, we will investigate it using subgroup analyses and sensitivity analyses. We will consider whether an overall summary is meaningful, and if it is, we will use random-effects analysis to produce it. We did not carry out our planned subgroup analyses, due to insufficient data. These will be carried out in future updates as more data become available. We will carry out the following subgroup analyses. (1) Gestational age (less than eight weeks and more than eight weeks), (2) Maternal age (less than 18 years, between 18 and 30 years and more than 30 years), (3) Type of surgical evacuation method used (any type of vacuum aspiration versus sharp metal curettage).

We will use the following outcomes in subgroup analysis: Women's satisfaction with procedure, Pain during or after surgical evacuation of miscarriage, or both and Maternal mortality.

For fixed-effect inverse variance meta-analyses, we will assess differences between subgroups by interaction tests. For random-effects and fixed-effect meta-analyses using methods other than inverse variance, we will assess differences between subgroups by inspection of the subgroups' confidence intervals; non-overlapping confidence intervals being indicative of a statistically significant difference in treatment effect between the subgroups.

Sensitivity analysis. In future updates, we will carry out sensitivity analysis to assess variability of global effect estimation, in order to modify the incorporation of the clinical trials to analysis, according to its methodological quality (low bias risk versus moderate or high risk) and discussing why studies have a larger influence on the estimate.

RESULTS

Description of studies

Results of the search. The search of the databases yielded 292 references. Cochrane Pregnancy and Childbirth Group's Trials Register, CENTRAL, PubMed, EMBASE, CINAHL and LILACS retrieved 6, 13, 34, 35, 10 and 194 reports respectively. After applying the inclusion and exclusion criteria, we selected 22 studies from the search result and discarded 270 reports. From those, we excluded 14 duplicates. At the end, we selected eight trials for full paper review and inclusion. One trial was excluded after the full paper review. For details of the study selection process see the study flow diagram (Figure 1).

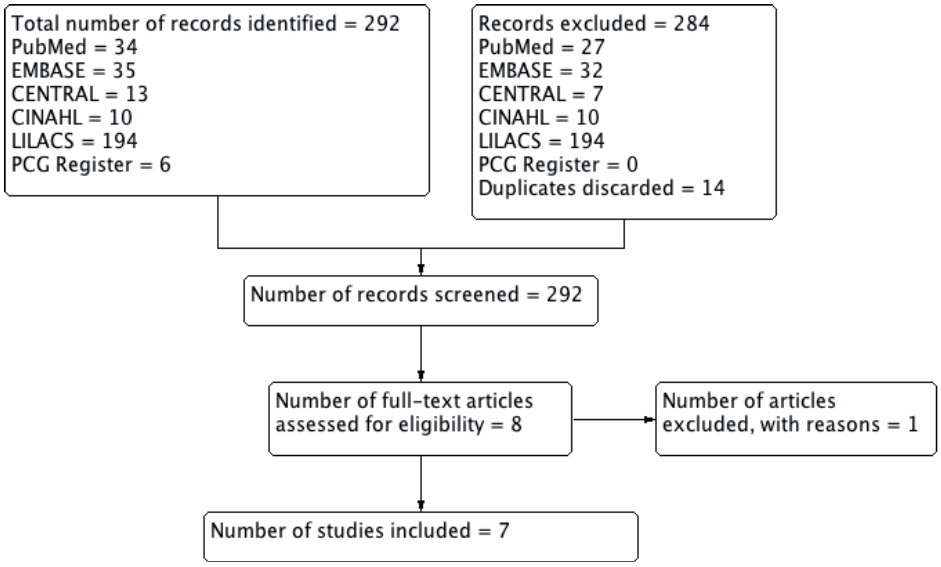

Figure 1. Study flow diagram.

Included studies. All the included trials used a randomised clinical trial design. Four of the trials were from developing countries; two were from the African continent (De Jonge 1994; Egziabher 2002), one from Panama (Lopez 2007) and one from Dominican Republic (Gomez 2004). From the remaining included studies, two were from United States (Kestin 1987; Rock 1977) and one was from Spain (Castillo 2004). Full details of all the included studies can be found in the Characteristics of included studies table.

One study did not have funding support (Egziabher 2002), one was supported by the David and Lucille Packard Foundation (Gomez 2004) and the others do not report any source of funding.

We included seven studies assessing different and diverse anaesthetic techniques on women with a prior diagnosis of incomplete miscarriage. All trials included participants with clinical or ultrasound diagnosis and up to 16 weeks of gestational age. One trial also included participants with missed abortions and anembryonic pregnancies (Lopez 2007). Most of the studies excluded women at high risk with cardiac, respiratory or other severe systemic disorders as well as women who were allergic to the anaesthetic drugs used. The majority of the studies selected women with open or dilated cervical canal and the most popular method used for the uterus evacuation was manual vacuum aspiration.

From these trials, we explored nine comparisons. Of them, three were related with PCB (Egziabher 2002; Gomez 2004; Lopez 2007). Two trials studied comparisons of sedation (with intravenous opioids and/or benzodiazepines at different doses) versus general

anaesthesia performed with induction agents, opioids and supported with halogens agents or nitrous oxide (De Jonge 1994; Rock 1977). Two studies explored comparisons between modalities of general anaesthesia using different drugs or doses (Castillo 2004). The last comparison was made between intramuscular (IM) NSAIDs and IM opioids (Lopez 2007). We have provided full details of the comparisons in the Characteristics of included studies table. Aditionally, Figure 2 illustrates the comparisons performed in the trials.

The most common outcome assessed was intra or postoperative pain measured in different ways. Two trials reported pain score as a continuous variable (using verbal numerical scales in the postoperative period) (Gomez 2004; Lopez 2007). Egziabher 2002 and De Jonge 1994 reported postoperative pain using a categorical scale with five levels (verbal rating scales). Castillo 2004 used a four-level categorical scale and Kestin 1987 and Rock 1977 did not report intra or postoperative pain.

One trial reported the quality of anaesthesia as a dichotomous result, according to participant rating (success or failure). This was assessed during the postoperative period (Rock 1977). No other studies reported women's satisfaction-related outcomes.

Six trials presented data of postoperative nausea or vomiting as a dichotomous result (Castillo 2004; Egziabher 2002; Gomez 2004; Kestin 1987; Lopez 2007; Rock 1977). Two trials reported the requirement of blood transfusion in the postoperative period (De Jonge 1994; Rock 1977). We found no trials that reported outcomes about mortality or other secondary or adverse effects.

To describe our results we classified the comparisons into four groups. In the first group, PCB was compared against other techniques. The second group presented comparisons between sedation and general anaesthesia. The third one compared diverse modalities of general anaesthesia and the fourth group with other comparisons.

The comparisons revealed a very high clinical heterogeneity and this represented a major issue in order to provide a single effect estimate for the outcomes. In fact, we organised the comparisons and the outcomes to improve the description of the findings. However, each comparison by itself was done with different drugs (with different pharmacological profiles), doses and routes of administration. For this reason, we did not perform any meta-analysis technique in this review.

Excluded studies. We excluded one trial because its participants were out of the scope of this review. For further details, see the Characteristics of excluded studies table.

Risk of bias in included studies

Allocation (selection bias). Of the seven trials, four were classified as having an adequate randomisation sequence generation (Gomez 2004; Egziabher 2002; Lopez 2007; Rock 1977) and the other three studies were rated as having 'unclear' risk of bias.

Table 1. Characteristics of included studies

Castillo 2004

Methods	This study was designed to determine which single bolus dose of remifentanil in combination with propofol and nitrous oxide is best to control the haemodynamic, autonomous and somatic responses in women scheduled for dilatation and curettage of the uterine cervix. They evaluated the adequacy of different bolus doses of remifentanil, associated with propofol and nitrous oxide, for dilatation and curettage in a prospective double-blind study.
Participants	Inclusion criteria: healthy females scheduled for dilation and curettage after spontaneous abortion were enrolled. Exclusion criteria: ASA classification III or worse, history of cardiac, pulmonary, endocrine, hepatic or renal disease, morbid obesity, neuropsychiatric disorders, antihypertensive medication, emergency curettage for massive bleeding or haemodynamic instability, age less than 18 years. Source: Hospital General Universitario Gregorio Marañón, Spain. Date: not reported.
Interventions	3 groups. - Group A. Remifentanil 0.5 mcg/kg single bolus intravenously plus propofol 2 mg/kg. Mantained with nitrous oxide 60% plus oxygen. - Group B. Remifentanil 1 mcg/kg single bolus intravenously plus propofol 2 mg/kg. Mantained with nitrous oxide 60% plus oxygen. - Group C. Remifentanil 1.5 mcg/kg single bolus intravenously plus propofol 2 mg/kg. Mantained with nitrous oxide 60% plus oxygen. Total number of participants randomised = 34. Group A = 4, Group B = 15, Group C = 15.
Outcomes	- Haemodynamic stability, autonomic, somatic signs of light anaesthesia. - Adverse events (hypotension, bradycardia). - Total dose of remifentanil and number of additional doses. - Emergence time. - Time to response to a single verbal command. - Postoperative pain. Reported as categorical data (none, light, moderate, severe). - Nausea/vomiting postoperative. As dichotomous outcome.
Notes	ASA classification: American Society of Anesthesiologists (ASA) Physical Status.

Castillo 2004: Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Women were assigned to 1 of the 3 groups according to the bolus dose of remifentanil to be administered".
Allocation concealment (selection bias)	Unclear risk	There is no information available.
Blinding (performance bias and detection bias)	Low risk	Blood pressure, heart rate and oxygen saturation were recorded by a blinded observer 1 minute before induction, at the end of propofol injection, during the first minute of curettage and just after completion of the procedure.
Incomplete outcome data (attrition bias)	Low risk	There is no description of incomplete data during follow-up period. As far as can tell, all patients appear to be evaluated.
Selective reporting (reporting bias)	Unclear risk	As far as can tell, outcomes reported were those pre-specified, however the trial protocol was not assessed.
Other bias	Low risk	No apparent biases from other sources.

De Jonge 1994

Methods	Randomised clinical trial to test the following hypotheses: (i) evacuation under systemic analgesia for uncomplicated incomplete abortion is safe, effective and acceptable; (ii) the delay between admission and the evacuation procedure is shorter for ward evacuations than for evacuations done in theatre; and (iii) blood loss for the ward group is less than for the theatre group.
Participants	Inclusion/exclusion criteria: uterine size equivalent to a pregnancy duration of 14 weeks or less, a dilated cervical canal, a haemoglobin concentration more than 8 g/dL after resuscitation and no signs of sepsis (temperature > 37.5°C, foul-smelling vaginal discharge). No women refused to participate. Source: Kalafong Hospital, a tertiary medical centre serving a black urban population. University of Pretoria. Date: between February and May 1992.
Interventions	2 groups. - Group 1. Sedation: It was provided by an opioid analgesic, fentanyl, and a benzodiazepine, midazolam. For the ward evacuation, the analgesic technique was as follows: pre-oxygenation for at least 3 minutes with 6-7 litres oxygen delivered through a close-fitting mask; fentanyl 1.5 mcg/kg given slowly intravenously up to a maximum of 100 mcg/kg, followed by midazolam administered slowly intravenously and titrated against the consciousness level of the participant to a maximum of 15 mg. Oxygenation was monitored by pulse-oximetry for the entire procedure. - Group 2. General anaesthesia. The anaesthetic technique for the evacuation in theatre was: pre-oxygenation; thiopental. 3.0-5.0 mg/kg intravenously, succinyldicholine 1.0 mg/kg intravenously; routine intubation because none of the women were starved; inhalation of oxygen and nitrous oxide (50/50) 70 ml/kg and halothane 0.5% to 1.0% with spontaneous respiration. • All the evacuations, both in the ward and in theatre, were performed with a sharp curette by a trained house officer or registrar. Total number of participants randomised = 142. Group 1 = 73, Group 2 = 68.
Outcomes	- Time delay between admission and evacuation. - Complications (anaesthetic- and procedure-related). - Acceptability, measured retrospectively by the level of fear and/or pain experienced by the woman grading: 1 - none; 2 - mild; 3 - moderate; 4 - severe; 5 - very severe. - Requirement for blood transfusion. - Need for re-evacuation.

De Jonge 1994: Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	There is no information available.
Allocation concealment (selection bias)	Low risk	"Randomisation was done using numbered sealed opaque envelopes drawn by the clinician on a consecutive basis".
Blinding (performance bias and detection bias)	Unclear risk	There is no information available.
Incomplete outcome data (attrition bias)	Unclear risk	There is no information available.
Selective reporting (reporting bias)	Unclear risk	Appears to be free of selective reporting bias but we did not assess the trial protocol.
Other bias	High risk	The number of women was less than the number calculated in the protocol. Quote: "The sample size of 182 could not be achieved because of hospital strikes and unrest".

Egziabher 2002

Methods	Randomised clinical trial comparing PCB with lidocaine versus placebo in the control of pain during manual vacuum aspiration.
Participants	Inclusion criteria: women with diagnosis of incomplete miscarriage before 16 weeks of gestation. Participants without evidence of infections, blood pressure less than 140/90 mmHg, non-diabetic or cardiac disease, free from severe anaemia, cervical dilation at least 1.5-2 cm and free from acute pelvic inflammatory disease. Exclusion criteria: abortion occurring 16 weeks and over of gestation, blood pressure greater or equal to 140/90 mmHg, infections of cervix, uterus and pelvis, diabetic and cardiac disease, allergy to lidocaine and respiratory distress. Source: Marie Stopes Health Centres, Nairobi, Kenia. Date: period from September 1997 to October 1997.
Interventions	2 groups. - Group 1. PCB (2 mL of lidocaine injection at the cervical-vaginal juncture at 3 and 9 o'clock positions). - Group 2. PCB (2 mL of normal saline solution injection at the cervical-vaginal juncture at 3 and 9 o'clock positions). Total number of participants randomised = 142. Group 1 = 71, Group 2 = 71.
Outcomes	- Postoperative pain. Using Mc Gill scale (none pain, mild, moderate, severe, very severe). The assessment was performed before, during, after and 30 minutes after the end of surgical procedure. The results are reported as categorical data. - Postoperative nausea-vomiting. Reported as dichotomous outcome.
Notes	PCB: Paracervical block

Egziabher 2002: Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"142 randomly selected participants, using random tables".
Allocation concealment (selection bias)	Unclear risk	There is no information available.
Blinding (performance bias and detection bias)	Low risk	The investigator, participant and the nurse filling out the questionnaire were blinded to allocation. 1 nurse who gave out the medication was not blinded.
Incomplete outcome data (attrition bias)	Unclear risk	No loss of participants nor exclusions reported.
Selective reporting (reporting bias)	Unclear risk	Seems to be free of bias here. However, we did not assess the trial protocol.
Other bias	High risk	The reported results of McGill scale per each category does not add 100% per each arm of treatment.

Gomez 2004

Methods	To estimate the effectiveness of PCB in controlling pain among women treated with manual vacuum aspiration for an incomplete abortion. An open parallel, randomised clinical trial was designed comparing 2 groups.
Participants	Women attending Maternidad Nuestra Señora de la Altagracia who were diagnosed as having an incomplete abortion and who fulfilled all the selection criteria. Inclusion criteria: women with incomplete abortion, open cervix, and pregnancies of 12 weeks or less gestational age, women aged 18 to 45 years, women able to and capable of giving written informed consent. Exclusion criteria: women with septic abortion, psychiatric or neurological disease, hypovolaemic or septic shock, abdominal rebound pain or signs of peritonitis, allergies to lidocaine, any observable pelvic mass, previous enrolment in the study, a severe medical condition (neoplasia), live fetus in utero, suspicions or presence of a sexually transmitted infection. Source: women attending Maternidad Nuestra Señora de la Altagracia located in Santo Domingo, Dominican Republic. Date: period from April 2, 2002 to October 23, 2002.
Interventions	2 groups. - Group 1. Without anaesthesia. - Group 2. PCB with 1% lidocaine during manual vacuum aspiration. The PCB was performed with a 23-gauge needle used to inject 5 mL of lidocaine slowly to a depth of 0.5 cm in the cervix–vaginal joint at 4- or 5- and 7- or 8-o'clock positions. All participants received counselling and psychological support before, during and after the procedure. Used a total of 10 mL of lidocaine (5 mL in each site). 5 minutes after applying the lidocaine, the gynaecologist, using the manual vacuum aspiration technique, evacuated the uterus. Total number of participants randomised = 215. Group 1 = 108, Group 2 = 107.
Outcomes	- Intraoperative pain as evaluated by the woman and external observer. The pain expressed by the woman at various points of treatment also was measured both as a discrete variable and as a categorical variable: no pain (0 points) or slight pain (1–3 points), moderate pain (4–6 points), and severe pain (7–10 points). - Changes in the level of pain on the basis of a comparison of pain before the procedure and pain reported during the procedure. - The need to suspend the procedure or administer anaesthetics medicaments or parenteral sedatives; the need for other parenteral analgesics. - Existence of intraoperative and postoperative complications (infection, haemorrhage uterine perforation, and incomplete evacuation), the need for further surgery, the presence of adverse events, and the presence of serious adverse events.
Notes	PCB: Paracervical block

Gomez 2004: Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Women were assigned to 1 of the 2 groups by means of a random number table, generated by a computational algorithm based on a block size of 2 (20%), 4 (40%), and 6 (40%) to generate a list of treatment allocation.

Allocation concealment (selection bias)	Low risk	The randomisation distribution was kept in sealed, sequential opaque envelopes kept at the Reproductive Health Department's office at Maternidad Nuestra Señora de la Altagracia and only opened when a study participant had consented to the study and was in the operating theatre for treatment.
Blinding (performance bias and detection bias)	Low risk	Consenting participants were treated in the operating theatre, where the randomisation group assignment was opened to determine the pain control to be received. An external trained observer evaluated pain levels. The biostatistician responsible for processing and analysing data was blinded regarding the 2 groups being studied.
Incomplete outcome data (attrition bias)	Low risk	No losses and no exclusions were reported. All patients after randomisation were evaluated.
Selective reporting (reporting bias)	Unclear risk	Pre-specified outcomes reported on, but the trial protocol not assessed.
Other bias	Low risk	There was no other information which would suggest other biases.

Kestin 1987

Methods	This study was undertaken to compare the newer IV agents, alfentanil and etomidate with fentanyl and thiopental. Quality of recovery and the frequency of side effects were assessed.
Participants	Inclusion/exclusion criteria: Women presenting for evacuation of retained products of conception after spontaneous inevitable abortion (within 16 weeks of gestation) were studied. No participants had received any sedative or analgesic medication before the study. Source: Princess Anne Hospital, Southampton. Date: not reported.
Interventions	2 groups. - Group 1. General anaesthesia with fentanyl-thiopental. Fentanyl intravenous 1 mcg/kg followed after 2 minutes by an induction dose of thiopental (until loss of the eyelash reflex). Mantained with nitrous oxide 70% plus oxygen. - Group 2. General anaesthesia with alfentanil-etomidate group received alfentanil 10 mcg/kg followed immediately by an induction dose from a syringe containing etomidate 20 mg intravenous. Mantained with nitrous oxide 70% plus oxygen. Total number of participants randomised = 44. Group 1 = 22, Group 2=22.
Outcomes	- Recovery from anaesthesia. It was assessed using a modification of the coin counting test. 10 coins, 2 of each denomination less than 50 pence, were used. 3 coins were removed at random and the remaining 7 coins presented in a column to the participant, who was instructed to pick them from the top of the column 1 by 1, keeping a verbal. Reported as dichotomous outcome. - Time to opening eyes after procedure. Reported in minutes. - Time to showing thumb on command. Reported in minutes.

Kestin 1987: Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	They were then randomly allocated to receive either alfentanil and etomidate or fentanyl and thiopental.
Allocation concealment (selection bias)	Unclear risk	There is no information available.

Blinding (performance bias and detection bias)	Unclear risk	There is no information available.
Incomplete outcome data (attrition bias)	Unclear risk	There is no information available.
Selective reporting (reporting bias)	Unclear risk	Pre-specified outcomes reported on, but the trial protocol not assessed.
Other bias	Low risk	"There were no significant difference between the two groups in baseline characteristics".

Lopez 2007

Methods	The objective of this study was to compare the effectiveness and the adverse effects of analgesics most commonly used in daily practice for the treatment of incomplete abortion with MVA.
Participants	Inclusion criteria: women with ultrasound diagnosis of incomplete miscarriage before 12 weeks of gestation (53%). They also included women with missed abortions (35%) and anembryonic pregnancies (12%). The women were included once the uterine cervix was pharmacologically dilated. Exclusion criteria: women who had history of allergy to any of the analgesics used and participants who did not want to participate in the study. Source: women who attended the gynaecology department of the Complejo Hospitalario "Arnulfo Arias Madrid", Caja de Seguro Social, Panama. Date: period from March 1 to June 13, 2004.
Interventions	3 groups. - Group 1. IM diclofenac (1 mg/kg) plus PCB (1 mg/kg of lidocaine at the cervical-vaginal juncture at 3, 5, 7, and 9 o'clock positions). - Group 2. IM diclofenac (1 mg/kg) plus meperidine IM (1 mg/kg). - Group 3. IM meperidine (1 mg/kg) alone A latency period of at least 30 minutes was given before starting the procedure. All participants received psychological support before, during, and after the procedure. Total number of participants randomised = 113. Group 1 = 37, Group 2 = 39, Group 3 = 37.
Outcomes	1. Postoperative pain. Using Wong scale (visual analogue scale) ranked from 0 to 10. The assessment was performed 3 minutes after the end of surgical procedure. The results are reported as continuous and categorical data. 2. Postoperative nausea. Reported as dichotomous outcome.
Notes	IM: intramuscular. MVA: Manual vacuum aspiration. PCB: Paracervical block.

Lopez 2007: Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Women were assigned to the 3 groups by means of a random table generated by a computational algorithm based on a block size of 9, to generate a list of treatment allocation.
Allocation concealment (selection bias)	Low risk	The randomisation distribution was kept in sealed, sequential opaque envelopes, which were opened after admission and the analgesic was administered before the participant entered the operating room.
Blinding (performance bias and detection bias)	Unclear risk	The analgesic was administered before the participant entered the operating room. It is unclear for the outcome evaluation. It does not apply for the woman because it is a non-pharmacological intervention.

Incomplete outcome data (attrition bias)	Low risk	Of the 117 participants, 4 were excluded because of missing data including 1 woman who decided not to participate after randomisation. Of the 113 recruited, 37 participants were enrolled to group 1, 39 participants to group 2 and 37 participants to group 3.
Selective reporting (reporting bias)	Unclear risk	Seem to have reported all pre-specified outcomes, but we did not access the trial protocol.
Other bias	Low risk	There was nothing to suggest any other risk of bias.

Rock 1977

Methods	Prospective, randomised clinical trial seeks to compare the choice of analgesia and anaesthesia in women with early spontaneous incomplete or inevitable abortion, undergoing suction curettage with regards to pain relief, post procedure rehabilitation, and hospitalisation time.
Participants	Inclusion/exclusion criteria: women with diagnosis of uncomplicated spontaneous incomplete or inevitable abortion were included. Women without signs or symptoms of sepsis or history or findings suggestive of instrumentation was included. Women with at least 6 hours of fasting. Women with a uterus greater than 12 weeks of gestational size were excluded. Source: Duke University Medical Center, Durham, North Carolina. Date: period from January 1, 1973 to December 31, 1974.
Interventions	2 groups. - Group 1. Intravenous analgesia. Diazepam 10 mg intravenous given 5-10 minutes before the procedure and meperidine 0.5 to 0.8 mg per pound with promethazine 25 mg. - Group 2. General anaesthesia. Thyamilal 75-250 mg or thiopental sodium 200-250 mg intravenous with 70% nitrous oxide and 30% oxygen by mask. Cervical dilation was performed when advisable. Curettage was performed with a translucent suction curette of the aspirator. Total number of participants randomised = 115. Group 1 = 59, Group 2 = 56.
Outcomes	- Quality of anaesthesia and analgesia. As dichotomous result of success/failure. Failues were based on the lack of participant cooperativeness during the procedure and complaints of discomfort during and following surgery. - Participant evaluation of success/failure. As dichotomous result. - Time from procedure to discharge. - Time from admission to discharge.

Rock 1977: Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	On the basis of a card drawn from an index file in which the order of the cards had been previously mathematically randomised.
Allocation concealment (selection bias)	Unclear risk	There is no information available.
Blinding (performance bias and detection bias)	Unclear risk	There is no information available.
Incomplete outcome data (attrition bias)	Unclear risk	No losses and no exclusions were reported, but nothing is described.
Selective reporting (reporting bias)	Unclear risk	Appears to be free of selective reporting bias but we did not assess the trial protocol.
Other bias	Unclear risk	No imbalances in baseline data identified.

Randomised clinical trial	Comparisons performed	
Group 1. Comparisons incluiding PCB		
Egziabher 2002	PCB with lidocaine	PCB with saline solution
Lopez 2007	PCB plus IM diclofenac	IM diclofenac plus IM meperidine
Lopez 2007	PCB plus IM diclofenac	IM meperidine
Gomez 2004	PCB with lidocaine	No anaesthesia
Group 2. Comparisons of sedation versus general anaesthesia		
De Jonge 1994	Sedation: fentanyl plus IV midazolam	General anaesthesia: thiopental plus halothane
Rock 1977	Sedation: IV meperidine plus IV diazepam	General anaesthesia: thiopental plus nitrous oxide
Group 3. Comparisons of modalities of general anaesthesia		
Kestin 1987	General anaesthesia: etomidate, alfentanil and nitrous oxide	General anaesthesia: thiopental, fentanyl and nitrous oxide
Castillo 2004	General anaesthesia: propofol, remifentanil 1 mcg/kg	General anaesthesia: propofol, remifentanil 1.5 mcg/kg
Group 4. Other comparisons		
Lopez 2007	IM diclofenac plus IM meperidine	IM meperidine

Figure 2. Comparisons performed among trials.

Table 2. Characteristics of excluded studies

Grunstein 1976

Reason for exclusion	The participants of this study are out of the scope of this review. In this study, epidural analgesia was performed in 78 women with abortion in the midtrimester or preterm delivery of up to 27 weeks of pregnancy. Women were divided into 3 groups. The first group included 30 women with signs of inevitable abortion. The second group comprised of 9 cases of induced abortion and the third one of 39 cases of preterm delivery.

Allocation concealment was adequate in three studies (Gomez 2004; De Jonge 1994; Lopez 2007). For the remainder it was unclear.

Blinding (performance bias and detection bias). Three studies were categorised as 'low' risk of bias for blinding (Castillo 2004; Egziabher 2002; Gomez 2004). The remaining trials were rated as having an 'unclear' risk of bias for this domain.

Incomplete outcome data (attrition bias). Three studies were categorised as 'low' risk of bias for this domain (Gomez 2004; Lopez 2007; Castillo 2004). The remaining studies were classified as having 'unclear' risk of bias.

Selective reporting (reporting bias). It was unclear to us whether any of the studies were free of selective reporting bias as we were unable to assess the protocols for the studies.

Other potential sources of bias. Two trials (De Jonge 1994; Egziabher 2002) were classified as 'high' risk of bias. De Jonge 1994 was stopped early and failed to recruit the participants planned.

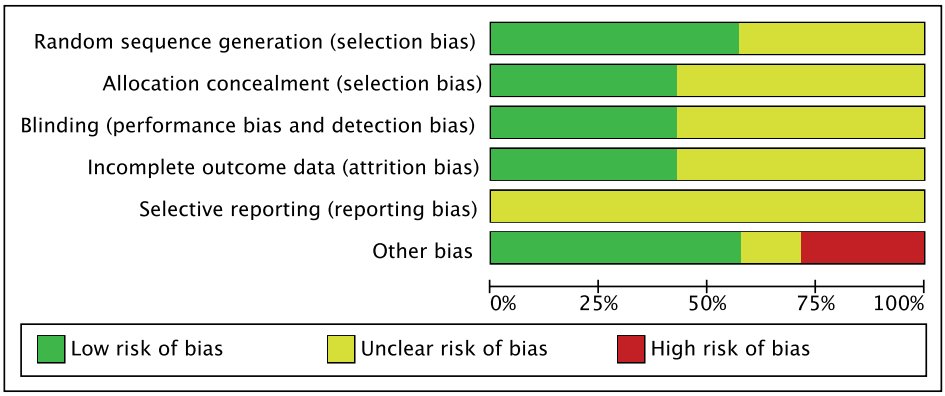

Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

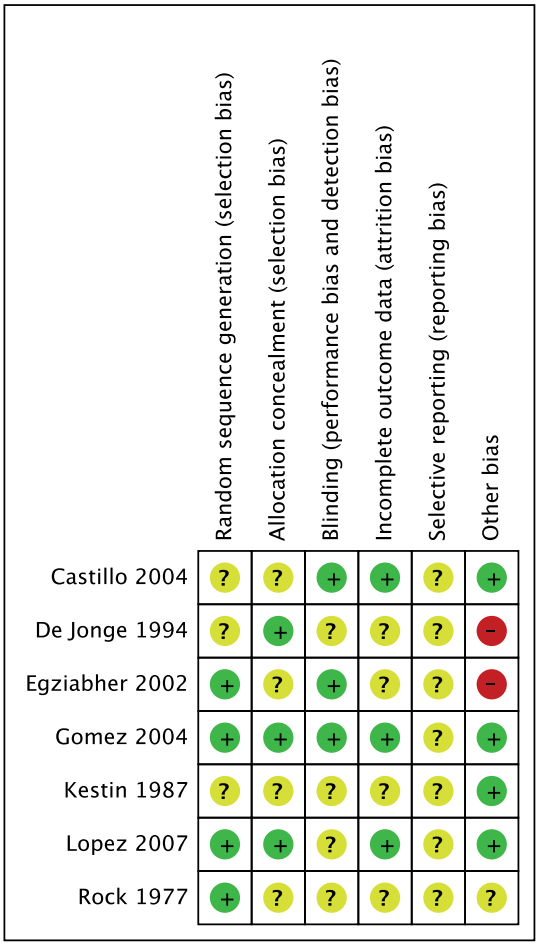

Figure 4. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

In conclusion, the trials included in this review have several risks of bias. The domain most achieved was adequate sequence generation. The remaining domains of evaluation were reached in less than 50% of the studies. We have included a summary of the 'Risk of bias' assessment in the Characteristics of included studies table, in the 'Risk of bias' graph (Figure 3) and in the 'Risk of bias' summary graph (Figure 4).

Effects of interventions

We present our results organised hierarchically by outcome. As mentioned above, we have four comparison groups. For more details please refer to (Figure 2). We show each category only where studies assessing the outcome were available.

Primary outcomes: Postoperative pain

Group 1 - comparisons including PCB

Egziabher 2002 compared the use of PCB with lidocaine versus block with saline solution. Significant differences favouring the group with lidocaine were found (moderate or severe postoperative pain) (risk ratio (RR) 0.32; 95% confidence interval (CI) 0.18 to 0.59 (Analysis 1.1)).

Lopez 2007 made two comparisons. In the first one, PCB plus IM diclofenac versus IM diclofenac plus IM meperidine, using the dichotomous outcome (moderate or severe postoperative pain) no significant differences were found (RR 0.98; 95% CI 0.73 to 1.30 (Analysis 2.1)). Furthermore, they reported a mean pain of 5.4 (standard deviation (SD) 2.8) (n = 37) and 5.0 (SD 2.6) (n = 39) respectively. No significant differences were found between these interventions (mean difference (MD) 0.40; 95% CI -0.82 to 1.62 (Analysis 2.2)).

In the other comparison, PCB plus IM diclofenac versus IM meperidine, using the dichotomous outcome (moderate or severe postoperative pain) no significant differences were found (RR 1.00; 95% CI 0.74 to 1.35 (Analysis 3.1)). They also reported a mean pain of 5.4 (SD 2.8) (n = 37) and 5.7 (SD 3.2) (n = 37) respectively. No significant differences were found between these interventions (MD -0.30; 95% CI -1.67 to 1.07 (Analysis 3.2)).

Gomez 2004 comparing PCB with lidocaine versus No anaesthesia/No sedation, reported no significant differences in moderate or severe postoperative pain (RR 1.00; 95% CI 0.86 to 1.16 (Analysis 4.1)). Similar results were reported using a continuous scale (MD -0.43; 95% CI -1.29 to 0.43 (Analysis 4.2)).

Group 2 - comparisons of sedation versus general anaesthesia

De Jonge 1994 compared a sedation strategy (intravenous (IV) fentanyl, IV midazolam) versus general anaesthesia (thiopental and halothane). No significant differences were found between these interventions (moderate or severe postoperative pain) (RR 0.07; 95% CI 0.00 to 1.23 (Analysis 5.1)).

Group 3. Comparisons of modalities of general anaesthesia

Castillo 2004 compared two bolus doses of remifentanil (1 mcg/kg versus 1.5 mcg/kg) with a fixed dose of propofol. No significant differences in moderate or severe postoperative pain were found between these interventions (RR 3.00; 95% CI 0.13 to 68.26 (Analysis 8.1)).

Group 4 - other comparisons

Lopez 2007 compared the effect of IM diclofenac plus IM meperidine versus IM meperidine alone. No significant differences were found between these interventions in moderate or severe postoperative pain (RR 1.02; 95% CI 0.77 to 1.36 (Analysis 9.1). The result was presented as a continuous scale with similar findings (MD -0.70; 95% CI -2.01 to 0.61 (Analysis 9.2)).

Primary outcomes: Women's satisfaction

Group 2 - comparisons of sedation versus general anaesthesia

Rock 1977 presented a comparison of general anaesthesia (thiopental, nitrous oxide) versus sedation (IV meperidine and IV diazepam). In terms of participant satisfaction, this study reported the outcome quality of anaesthesia (assessed by the woman). Significant differences were found between groups (RR 1.25; 95% CI 1.10 to 1.43 (Analysis 6.1)).

Secondary outcomes: Postoperative nausea and vomiting

Group 1 - comparisons including PCB

Egziabher 2002 showed a significant difference favouring the PCB with Lidocaine versus PCB with saline solution (RR 0.56; 95% CI 0.40 to 0.79 (Analysis 1.2)).

In the comparison of PCB plus IM diclofenac versus IM diclofenac plus IM meperidine, Lopez 2007 presented a significant difference favouring the PCB plus IM diclofenac group (RR 0.19; 95% CI 0.05 to 0.81 (Analysis 2.3)).

In the PCB plus IM diclofenac versus IM meperidine alone group, significant differences favouring the PCB plus IM diclofenac were found (RR 0.18; 95% CI 0.04 to 0.76 (Analysis 3.3)).

In the last comparison of this category (PCB with lidocaine versus No anaesthesia/No sedation) no events of nausea or vomiting were reported (Gomez 2004) (Analysis 4.3).

Group 2 - comparisons of sedation versus general anaesthesia

No significant differences were found between these interventions in the Rock 1977 trial (RR 0.26; 95% CI 0.03 to 2.29 (Analysis 6.2)).

Group 3 - comparisons of modalities of general anaesthesia

Kestin 1987 compared two modalities of general anaesthesia: etomidate plus alfentanil versus thiopental plus fentanyl. Significant differences were found favouring the thiopental-fentanyl combination (RR 0.22; 95% CI 0.05 to 0.91 (Analysis 7.1)).

Castillo 2004 compared two bolus doses of remifentanil with a fixed dose of propofol. They did not find significant differences (RR 3.00; 95% CI 0.13 to 68.26 (Analysis 8.2)).

Group 4 - other comparisons

Lopez 2007 found no significant differences between IM diclofenac plus IM meperidine versus IM meperidine alone (RR 0.95; 95% CI 0.47 to 1.92 (Analysis 9.3)).

Table 3. Data and analyses

1. PCB with lidocaine versus PCB with saline solution

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Postoperative pain (moderate or severe)	1	142	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.18, 0.59]
1.2 Nausea/vomiting	1	142	Risk Ratio (M-H, Fixed, 95% CI)	0.56 [0.40, 0.79]

2. PCB with lidocaine plus IM diclofenac versus IM diclofenac plus IM meperidine

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
2.1 Postoperative pain (moderate or severe)	1	76	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.73, 1.30]
2.2 Postoperative pain	1	76	Mean Difference (IV, Fixed, 95% CI)	0.40 [-0.82, 1.62]
2.3 Nausea/vomiting	1	76	Risk Ratio (M-H, Fixed, 95% CI)	0.19 [0.05, 0.81]

3. PCB with lidocaine plus IM diclofenac versus IM meperidine

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
3.1 Postoperative pain (none/ mild)	1	74	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.74, 1.35]
3.2 Postoperative pain	1	74	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-1.67, 1.07]
3.3 Nausea/vomiting	1	74	Risk Ratio (M-H, Fixed, 95% CI)	0.18 [0.04, 0.76]

4. PCB with lidocaine versus no anaesthesia/no sedation

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
4.1 Postoperative pain (moderate or severe)	1	215	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.86, 1.16]
4.2 Postoperative pain	1	215	Mean Difference (IV, Fixed, 95% CI)	-0.43 [-1.29, 0.43]

4.3 Nausea/vomiting	1	215	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable

5. General anaesthesia (thiopental, halothane) versus sedation (fentanyl, midazolam)

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
5.1 Postoperative pain (moderate or severe)	1	141	Risk Ratio (M-H, Fixed, 95% CI)	0.07 [0.00, 1.23]
5.2 Requirement of blood transfusion	1	141	Risk Ratio (M-H, Fixed, 95% CI)	1.98 [1.10, 3.57]

6.General anaesthesia (thiopental, nitrous oxide) versus sedation (meperidine, diazepam)

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
6.1 Quality of anaesthesia (satisfaction)	1	115	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [1.10, 1.43]
6.2 Nausea/vomiting	1	115	Risk Ratio (M-H, Fixed, 95% CI)	0.26 [0.03, 2.29]
6.3 Requirement of blood transfusion	1	115	Risk Ratio (M-H, Fixed, 95% CI)	3.16 [0.13, 75.94]

7. General anaesthesia (thiopental, fentanyl, nitrous oxide) versus general anaesthesia (etomidate, alfentanil, nitrous oxide)

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
7.1 Nausea/vomiting	1	44	Risk Ratio (M-H, Fixed, 95% CI)	0.22 [0.05, 0.91]

8. General anaesthesia (remifentanil 1 mcg/kg bolus, propofol) versus general anaesthesia (remifentanil 1.5 mcg/kg bolus, propofol)

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
8.1 Postoperative pain (moderate or severe)	1	30	Risk Ratio (M-H, Fixed, 95% CI)	3.00 [0.13, 68.26]
8.2 Nausea/vomiting	1	30	Risk Ratio (M-H, Fixed, 95% CI)	3.00 [0.13, 68.26]

9. IM diclofenac plus IM meperidine versus IM meperidine

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
9.1 Postoperative pain (moderate or severe)	1	76	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.77, 1.36]
9.2 Postoperative pain	1	76	Mean Difference (IV, Fixed, 95% CI)	-0.70 [-2.01, 0.61]
9.3 Nausea/vomiting	1	76	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.47, 1.92]

Secondary outcomes: Requirement of blood transfusion

Group 2 - comparisons of sedation versus general anaesthesia

De Jonge 1994 compared a sedation strategy (IV fentanyl, IV midazolam) versus general anaesthesia (thiopental and halothane). They found significant differences favouring the general anaesthesia arm (RR 1.98; 95% CI 1.10 to 3.57 (Analysis 5.2)).

Rock 1977 reported no significant differences between groups (RR 3.16; 95% CI 0.13 to 75.94 (Analysis 6.3)).

DISCUSSION

The surgical management of an incomplete miscarriage is a common procedure in the practice of clinical anaesthesia. However, the different techniques currently used have not been evaluated through systematic methods and there is at present no consensus about the method or technique to provide better outcomes for women under this procedure.

This review examined randomised controlled trials comparing any anaesthetic technique (general anaesthesia, sedation/analgesia, regional or PCB) in this special type of population. We included seven trials in this review, but the information available in this area remains scarce.

Summary of main results

None of the included studies reported data about maternal mortality. One study reported maternal satisfaction (Rock 1977). In this trial, significant differences were found favouring the use of general anaesthesia in comparison with sedation/analgesia. However, this trial was classified with unclear risk of bias in five of six domains.

The included studies used different approaches to assess the outcome of postoperative pain. Five studies reported data related to postoperative pain. Three studies (Castillo 2004; De Jonge 1994; Egziabher 2002) used ordinal categorical scales with four or five categories. The remaining two trials (Gomez 2004; Lopez 2007) used continuous and categorical scales.

PCB does not improve the control of postoperative pain when it is compared against sedation/analgesia or versus no anaesthesia/no analgesia (Gomez 2004; Lopez 2007). When it is compared with PCB with saline solution, the women under block with lidocaine present less moderate or severe postoperative pain (Egziabher 2002). Nowadays, the postoperative pain level of women under surgical evacuation of incomplete miscarriage remain without complete relief.

For secondary outcomes, six trials reported the outcome nausea and vomiting (Castillo 2004; Egziabher 2002; Gomez 2004; Kestin 1987; Lopez 2007; Rock 1977) and two stud-

ies reported the need for postoperative blood transfusion (De Jonge 1994; Rock 1977). The results show a consistent finding. When opioid drugs were compared versus other strategies, these participants had more events of nausea and vomiting (Lopez 2007). In addition, when both arms has opioids the differences disappear (Castillo 2004). Kestin 1987 show a reduction in the risk of nausea and vomiting using a combination of general anaesthesia using thiopental, fentanyl versus etomidate, alfentanil (one trial, 44 participants). In the PCB scenario, the risk of postoperative nausea and vomiting was reduced using local anaesthetics versus saline solution (Egziabher 2002).

De Jonge 1994 reported a significant increment on the risk of blood transfusion with general anaesthesia versus sedation/analgesia. Nevertheless, Rock 1977 does not report any difference between general anaesthesia and sedation/analgesia. However, both studies used different drugs. In addition, the result presented by De Jonge 1994 could be influenced by the comparison under study. Patients allocated to sedation in the ward probably were evacuated more quickly than patients in the operating room under general anaesthesia.

Overall completeness and applicability of evidence

We included seven trials involving 800 women. Although we had planned to combine the estimates, explore the sources of heterogeneity and to carry out a subgroup/sensitivity analysis, the available studies and their comparisons allowed only a descriptive systematic review without meta-analysis. However, it shows an interesting overview of the great amount of heterogeneity in the clinical practice of anaesthesia.

From these seven trials, we evaluated nine comparisons. Four included PCB versus other modalities of anaesthesia and the remaining five included general anaesthesia versus sedation/analgesia or other type of general anaesthesia. No trials were found that compared PCB versus general anaesthesia.

The most frequent primary outcome reported was postoperative pain. It was reported in different ways using categorical or continuous scales. Only one study reported maternal satisfaction with the anaesthesia. No trials were found that reported maternal mortality with the procedure. From all trials, six reported postoperative nausea and vomiting and two reported postoperative requirement of blood transfusion.

Most women included in this review were diagnosed with incomplete miscarriage and the evacuation was done using manual vacuum aspiration or curettage. Only one trial included patients with missed abortions and anembryonic pregnancies.

Quality of the evidence

The quality of the evidence was intermediate. Only one of the seven included studies (Gomez 2004) was rated as being low risk of bias in six of seven domains of the risk of bias tool. Of the remaining six trials, four have an adequate sequence generation and

three had adequate allocation concealment. Also, of these six trials, three reported some form of blinding. In addition, it is hard to assess if there was selective reporting bias.

The risk of bias of the trial that reported an increase in the requirement of blood transfusion was unclear or high in several domains.

Potential biases in the review process

We attempted to minimise serious bias by the following; two review authors assessed eligibility for inclusion and two authors carried out data extraction and assessed risk of bias. Data entry into RevMan (RevMan 2008) was undertaken by one author. However, many of these steps involve subjective assessments and thus may carry some risk of bias.

Agreements and disagreements with other studies or reviews

We are unaware of other systematic reviews on this specific clinical question.

AUTHORS' CONCLUSIONS

Implications for practice

The evidence found presents conflicting results with the use of PCB. Most trials do not show differences with use of PCB. Unfortunately, in this anatomical area, it is difficult to assess the effectiveness and quality of the block. However, the pain perception remains significant among these patients. In addition, significant results shown by Egziabher 2002 in terms of pain could be explained by placebo effect taking into account that the Gomez 2004 trial comparison with no treatment failed to show an effect.

One trial suggested that women's satisfaction could be improved using general anaesthesia. The use of perioperative opioids was associated with an increase of postoperative nausea and vomiting in this scenario.

Key factors that influence the choice of anaesthesia for this procedure include availability, effectiveness, safety, side effects, practitioner choice and costs. These considerations should continue to be used to select the individual approach to each patient until more evidence is available. Furthermore, it is also important to consider the woman's preferences after anaesthesiologist advice about each technique.

Implications for research

Researchers in all medical specialties are increasingly studying non-traditional, patient-centred outcomes such as patient satisfaction and quality of life to assess quality of health care. Only one study examined this type of outcome and they did so in a very simple way (Rock 1977). Currently, we know that the assessment of patient satisfaction is a complex procedure because satisfaction is a multi-dimensional concept with determi-

nants that are not yet clearly defined (Pascoe 1983). Many studies use only simple overall questions and the reliability of single-item global satisfaction is poor and inadequate to address the complexity of satisfaction (Chanthong 2009; Fung 1998; Ware 1983).

Valid and reliable assessment of pain is essential for both clinical trials and pain management in clinical practice. One-dimensional tools such as numeric rating scales or visual analogue scales are available. Both are more powerful in detecting changes in pain intensity than a verbal categorical rating scale. In addition, it can be very useful to use baseline assessments to detect meaningful treatment effects (Breivik 2008).

To conclude, we consider that further studies in this context should be conducted. It should address important patient-oriented outcomes (i.e. patient satisfaction). In terms of pain management, appropriate methods to assess acute and long-term pain should be used. These trials should be large enough and well conducted. We identified several comparisons in our review process. With our current pharmacological agents and the development of anaesthetic methods, probably several forms could be available to perform this procedure nowadays.

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APPENDIX

Table. Search strategies

CENTRAL search strategy. The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2012, Issue 1).
#1 (incomplete near miscarr*)
#2 (incomplete near abort*)
#3 MeSH descriptor Abortion, Spontaneous explode all trees
#4 products near conception
#5 (rpoc)
#6 MeSH descriptor Anesthesia explode all trees
#7 anesthe* or anaesthe*
#8 MeSH descriptor Anesthetics explode all trees
#9 (#1 OR #2 OR #3 OR #4 OR #5)
#10 (#6 OR #7 OR #8)
#11 (#9 AND #10)
PubMed search strategy (1966 to 23 January 2012)
#1 "Abortion, Spontaneous"[Mesh]
#2 "Anesthetics"[Mesh]
#3 "Anesthesia"[Mesh]
#4 #2 OR #3
#5 #1 AND #4
#6 randomized controlled trial [pt]
#7 controlled clinical trial [pt]
#8 randomized [tiab]
#9 placebo [tiab]
#10 drug therapy [sh]
#11 randomly [tiab]
#12 trial [tiab]
#13 groups [tiab]
#14 #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13
#15 animals [mh] NOT (humans [mh] and animals [mh])
#16 #14 AND #5
#17 #16 NOT #15
EMBASE search strategy (1974 to 23 January 2012, via OVID)
1 exp Abortion/
2 incomplete miscarr*.ti,ab.
3 exp Anesthesia/
4 exp Anesthetic agent/
5 1 or 2
6 3 or 4

7 5 and 6
8 Clinical trial/
9 Randomized controlled trials/
10 Random Allocation/
11 Single-Blind Procedure/
12 Double-Blind Procedure/
13 Cross-Over Procedure/
14 Placebos/
15 Randomi?ed controlled trial$.tw.
16 RCT.tw.
17 Random allocation.tw.
18 Randomly allocated.tw.
19 Allocated randomly.tw.
20 (allocated adj2 random).tw.
21 Single blind$.tw.
22 Double blind$.tw.
23 ((treble or triple) adj blind$).tw.
24 Placebo$.tw.
25 Prospective Studies/
26 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25
27 Case study/
28 Case report.tw.
29 Abstract report/ or letter/
30 27 or 28 or 29
31 26 not 30
32 animal/ not human/
33 7 and 31
34 33 not 32
CINAHL search strategy. (1982 to 23 January 2012)
1 exp Abortion, spontaneous/
2 incomplete adj2 miscarr*
3 exp Anesthesia/
4 exp Anesthetics/
5 1 or 2
6 3 or 4
7 5 and 6
LILACS search strategy (searched 23 January 2012)
First block

((Pt ENSAIO CONTROLADO ALEATORIO OR Pt ENSAIO CLINICO CONTROLADO OR Mh ENSAIOS CONTROLADOS ALEATORIOS OR Mh DISTRIBUICAO ALEATORIA OR Mh MÉTODO DUPLO-CEGO OR Mh MÉTODO SIMPLES-CEGO) AND NOT (Ct ANIMALS AND NOT (Ct HUMANO AND Ct ANIMALS)) OR (Pt ENSAIO CLÍNICO OR Ex E05.318.760.535$) OR (Tw clin$ AND (Tw trial$ OR Tw ensa$ OR Tw estud$ OR Tw experim$ OR Tw investiga$)) OR ((Tw singl$ OR Tw simple$ OR Tw doubl$ OR Tw doble$ OR Tw duplo$ OR Tw trebl$ OR Tw trip$) AND (Tw blind$ OR Tw cego$ OR Tw ciego$ OR Tw mask$ OR Tw mascar$)) OR Mh PLACEBOS OR Tw placebo$ OR (Tw random$ OR Tw randon$ OR Tw casual$ OR Tw acaso$ OR Tw azar OR Tw aleator$) OR (Mh PROJETOS DE PESQUISA) AND NOT (Ct ANIMALS AND NOT (Ct HUMANO AND Ct ANIMALS)) OR (Ct ESTUDO COMPARATIVO OR Ex E05.337$ OR Mh SEGUIMENTOS OR Mh ESTUDOS PROSPECTIVOS OR Tw control$ OR Tw prospectiv$ OR Tw volunt$ OR Tw volunteer$) AND NOT (Ct ANIMALS AND NOT (Ct HUMANO AND Ct ANIMALS))) AND NOT Mh ANIMALS
Second block
Mh Abortion OR Mh Curettage OR Mh Miscarriage OR Mh miscarry$ OR abort$ OR surgical abortion OR abortion OR manual suction aspiration OR electric suction aspiration OR first trimester
Third block
Mh Thiopental OR Mh Propofol OR Mh Ketamine OR Mh Lidocaine OR Mh Bupivacaine OR thiop$ OR sodip$ OR pento$ OR tiop$ OR propof$ OR dipriv$ OR keta$ OR remifen$ OR remyfen$ OR Mh fentanyl OR narcot$ OR Mh morphine OR trama$ OR midazolam OR diazepam OR sedat$ OR anxiolyt$ OR Mh Nitrous oxide OR Sevo$ OR Isof$ OR Halot$ OR Enflu$ OR general ane$ OR general anae$ OR conduct$ OR region$ OR spin$ OR lidoc$ OR lydo$ OR xilo$ OR xylo$ OR bupiv$ OR bupyv$ OR bupi$
The three blocks were combined with 'AND'

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Chapter 6

Hemodynamic effects of a right lumbar–pelvic wedge during spinal anesthesia for cesarean section.

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ABSTRACT

Background

Aortocaval compression is a major cause of maternal hypotension. A randomized controlled trial was designed to determine the effectiveness of a mechanical intervention using a right lumbar-pelvic wedge in preventing hypotension after spinal anesthesia for cesarean delivery.

Methods

Eighty healthy women undergoing elective cesarean section were randomly allocated immediately after spinal blockade to either a lumbar-pelvic wedge positioned under the right posterior-superior iliac crest (Wedge group, n=40) or the complete supine position (Supine group, n=40). Hemodynamic values, vasopressor consumption and adverse effects were collected during the surgical procedure. Hypotension was defined as a reduction in systolic blood pressure of 25% from baseline. Patient allocation, management and data collection were performed by a single unblinded anesthetist.

Results

There was no difference in the incidence of hypotension between the two groups (42.5% vs. 50%, P=0.51). During the first 5 min, blood pressure decreased less in the Wedge group. There were significant differences in median [interquartile range] vasopressor requirements between the Wedge group and the Supine group (1 [0-2] vs. 3 [1-4] mg, P<0.01) and in nausea during the procedure (6 vs. 22 patients, P<0.01).

Conclusion

In our study population the use of right lumbar-pelvic wedge was not effective in reducing the incidence of hypotension during spinal anesthesia for cesarean section. Patients in whom the wedge was used had higher systolic blood pressure values during the first 5 min of anesthesia and fewer episodes of nausea. The risk of hypotension remains substantial.

Keywords

Spinal anesthesia; Cesarean section; Left lateral displacement; Right lumbar–pelvic wedge; Hypotension

INTRODUCTION

Spinal anesthesia for cesarean delivery can result in both maternal and neonatal morbidity. (1-4) Hypotension has a sudden onset and has been reported to occur with a frequency approaching 100%. (5,6) It is caused by sympathetic block and increased venous capacitance which, together with inferior vena caval compression by the gravid uterus, leads to pooling of blood in the lower extremities, preload reduction and hemodynamic compromise. (7)

Several strategies to maintain blood pressure have been studied, such as crystalloid/colloid pre- or co-loading, prophylactic use of vasopressors, low doses of spinal anesthetic and patient positioning. (1) A recent systematic review compared eight positions during the surgical procedure but failed to reach definite conclusions. (8) In our daily clinical practice, the supine position is used in almost all patients, although some anesthesiologists use saline solution bags under the right lumbar–pelvic area to promote left uterine displacement. A right lumbar–pelvic wedge was designed to simulate this approach and make it reproducible. The aim of the study was to evaluate if the use of a right lumbar–pelvic wedge during cesarean delivery under spinal anesthesia reduced the incidence of perioperative maternal hypotension.

METHODS

Ethical approval from Ethics Committee of Universidad del Cauca was granted. All patients gave written informed consent. ASA 1 or 2 patients aged between 18 and 45 years with an uncomplicated singleton pregnancy at term who were scheduled for cesarean delivery under spinal anesthesia were eligible for recruitment.

Exclusions were those with pregnancy-induced hypertension, cardiac disease, diabetes, fetal complications and those in labor. Post hoc exclusions were those in whom surgery lasted longer than 2 h, those who required perioperative sedation or conversion to general anesthesia, those in whom surgical complications arose such as intraoperative hemorrhage and those in whom protocol violation occurred.

Pre-medication was not given. Standard monitoring included non-invasive blood pressure measurements, pulse oximetry and electrocardiography. Baseline blood pressure and maternal heart rate were recorded. Oxygen was administered to all patients via nasal prongs at 3 L/min. An 18-gauge cannula was inserted in a forearm vein. All patients received co-loading with 0.9% saline 10 mL/kg. Spinal anesthesia was performed in the left lateral position at the L2–3 or L3–4 interspace with a 26-gauge Quincke spinal needle. All patients received 0.5% hyperbaric bupivacaine 9 mg and fentanyl 20 mcg (total volume 2 mL).

After intrathecal injection, patients were immediately placed in the supine position either with the right lumbar–pelvic wedge (Wedge group) or without (Supine group). Groups were assigned by an independent anesthetist using random numbers generated by EPIDAT 3.1. The wedge used was wood, 35 cm long, 20 cm wide and with 20° of inclination, and was placed at the right posterior–superior iliac crest and lumbar region. Spinal anesthesia, patient positioning, anesthetic management and data collection were performed by an unblinded anesthetist. The upper level of sensory block 15min after spinal injection was determined using loss of pinprick and cold sensation. Surgery began when the sensory block reached the T6 dermatome bilaterally.

Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and heart rate (HR) were collected minutely for the first 8 min, then every 3 min until 20 min, and every 5 min until the end of surgery. Maternal hypotension was defined as a 25% reduction of SBP from baseline, (1,9) and was treated with intravenous boluses of ethylephrine 1 mg until hypotension was corrected. Bradycardia (<40 beats/min) was treated with intravenous atropine 1 mg to a maximum dose of 3 mg. Vasopressor and atropine requirements were recorded. Any further management was at the clinical discretion of the anesthetist. The presence or absence of nausea and vomiting after spinal anesthesia were recorded.

Statistical analysis

The primary outcome was the incidence of hypotension during surgery. Secondary outcomes were vasopressor consumption and adverse effects. Power analysis revealed that 39 cases were required to show a decrease in the cumulative incidence of hypotension from 80% to 50% between groups with a level of 0.05 and b level of 0.2 using a two-tailed test. A low dropout rate was anticipated.

Continuous data were reported as mean (±SD) and categorical data were reported as numbers and percentages. SBP data are shown as bean plots, which were used to show the mean and data distributions at each measurement over time. (10) Nonparametric data were reported as median and interquartile range (IQR). Data between groups were compared using the t test, Mann–Whitney U test, X^2 test and Fisher's exact test as appropriate.

Sequential measurements of SBP were focused on the first 5 min, being the interval during which SBP showed most changes in graphical analysis. Analysis was per- formed using the area under the curve (AUC) of SBP for each patient as a summary statistic. AUC was calculated in sections using standard formulae for areas of rectangles and triangles, (11,12) and AUC results between randomization groups were compared using t test and presented as mean difference with 95% confidence intervals (95% CI).

In all cases, $P < 0.05$ was considered significant. All analyses and graphs were performed using the computer programs SPSS (version 15; Chicago, IL) and R project. (13) Data analysis was performed by an independent researcher who was blinded to the study interventions.

RESULTS

There were no protocol violations, dropouts or missing data. Eighty patients were enrolled in the study, with 40 in each group. There were no significant differences in demographic data between the groups, the extent of sensory blockade, the duration of surgery or ASA status (Table 1).

Hemodynamic baseline values did not differ between groups (Table 2). The incidence of hypotension was similar: 42.5% in Wedge group vs. 50% in Supine group (RR 0.7, 95% CI 0.3–1.7; P = 0.51). The distribution of SBP over time is presented in Fig. 1. During the first 5 min after spinal anesthesia, SBP, DBP and MAP decreased relative to baseline values in both groups. The AUC of SBP was 593 mmHg min and 540 mmHg min for the Wedge and Supine Groups, respectively (mean difference -52.97, 95% CI -85.19 to -20.75; P = 0.002). Thereafter, SBP, DBP and MAP increased slowly but did not reach baseline values in either group. There were no differences in maternal heart rate after the onset of spinal anesthesia. There were, however, significant differences in vasopressor median [IQR] requirements between the Wedge group and Supine group (1 [0–2] vs. 3 [1–4] mg, respectively; P < 0.01) and the incidence of nausea during the procedure (6 and 22 patients, respectively; P < 0.01).

Table 1. Maternal, obstetric and anesthetic data

	Wedge group (*n* = 40)	Supine group (*n* = 40)
Age (years)	29 (±7)	28 (±7)
Weight (kg)	70 (±8)	69 (±8)
Sensory block level	T5 [T4–T6]	T4 [T3–T6]
Duration of surgery (min)	42 [32–57]	45 [30–53]
ASA status		
I	23	25
II	17	15

Data are mean (±SD), median [range] or number; No significant differences between groups.

Table 2. Maternal hemodynamic data, vasopressor consumption and adverse effects

	Wedge group (*n* = 40)	Supine group (*n* = 40)	*P* value
Baseline systolic BP (mmHg)	130 (±17)	125 (±13)	0.16
Baseline mean BP (mmHg)	91 (±14)	86 (±11)	0.08
Baseline heart rate (beats/min)	83 (±12)	81 (±11)	0.45
Cumulative incidence of hypotension	17/40 (42.5%)	20/40 (50%)	0.51
Ethylephrine consumption (mg)	1 [0–2]	3 [1–4]	0.01
Atropine consumption (mg)	0 [0–0]	0 [0–0]	0.15
Nausea	6	22	0.01
Vomiting	0	4	0.11

Data are mean (±SD), median [range] or number.

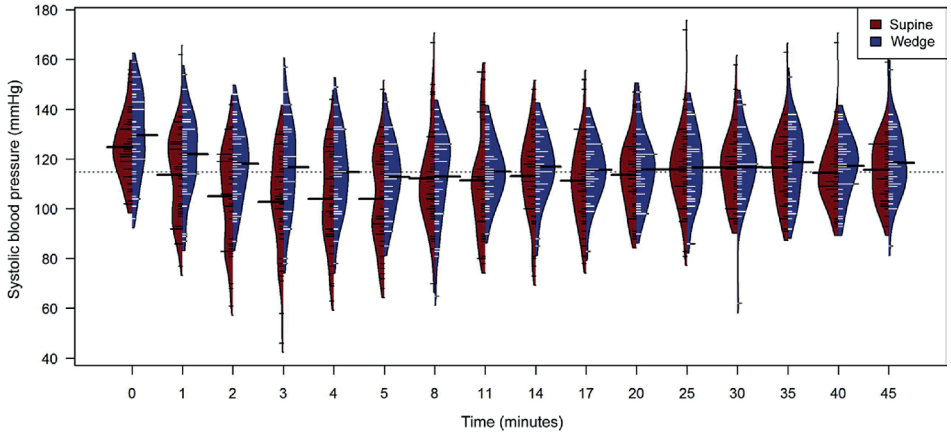

Figure 1. Systolic blood pressure distribution following spinal anesthesia. The graph represents the distribution of the values for systolic blood pressure at each time point and per intervention group. The thick black line represents the mean value for each distribution.

DISCUSSION

Several authors have studied the effect of positioning following induction of spinal or combined spinal–epidural anesthesia for cesarean section. The studies are in three main categories. The first compares the left or right tilted supine position with the full left lateral position. (14-17) The second compares lateral or tilted supine positions with the complete supine position, (18-21) and the third compares different locations of wedges or right-tilted vs. left-tilted positions. (22,23) The current study could be classified in the last of these three groups because it compared the use of a lumbar–pelvic wedge with the complete supine position. The results show that hypotension occurred frequently and that the wedge used was ineffective in reducing the incidence of maternal hypotension, but that patients with the wedge required less vasopressor and experienced fewer episodes of nausea.

Matorras et al. assessed the benefits of performing cesarean delivery under spinal or general anesthesia using lateral tilt or supine position. (20) No differences in blood pressure control, umbilical artery biochemistry or clinical condition of the newborn were shown. Comparisons with our study are limited due to the patient populations, but similar incidences of hypotension were found.

The Cardiff wedge was initially designed to perform maternal resuscitation. (24) It is a rigid wedge with an upper plane angled at 27°, the maximum tilt found to be consistent with effective external cardiac massage. Crawford et al. observed that compared to the supine position, right lateral tilt for uterine displacement improved neonatal outcome during general anesthesia for cesarean delivery, and attributed this finding to the management of inferior vena caval occlusion. They suggested that the use of a wedge or

some tilting device was advisable, although conceded that left tilt was preferable. (19) In the current study the wedge covered the lumbar and pelvic region but was shorter than the original Cardiff wedge and had only 20° of inclination. Theoretically, this position relieves aortocaval compression but it is difficult to estimate the extent of uterine displacement. (25) A recent systematic review did not show differences in maternal blood pressure between left or right lateral and complete supine positions. (21)

In the present study, prophylactic vasopressors were not used, the anesthetic technique was standardized and the upper level of anesthesia was similar in both groups. The only a_1 vasopressor available in the operating rooms of our institution is ethylephrine, which may produce tachycardia through b_1 stimulation as a secondary effect. Although the incidence of hypotension was the same in both groups, SBP in the Supine group showed a more rapid fall over the first 5 min, and differences in the AUC of the SBP between groups favored the Wedge group. Zhou et al. found higher SBP during the first min in patients using a lumbar wedge versus a pelvic wedge. (22) The clinical relevance of this finding and its relationship to nausea and vomiting are unknown.

The incidence of hypotension varies according to its definition and limits comparability of different preventive measures. (9) We used a commonly accepted definition, and the incidence was high but in agreement with other studies. (1,26) Current evidence for the prevention of hypotension during cesarean delivery with spinal anesthesia suggests that an approach employing vasopressor infusions, co-loading fluids and positioning may be the best strategy. (27,28) Other authors have concluded that, despite a high incidence of maternal hypotension during cesarean delivery, term infants tend to tolerate the physiological insult without major sequelae. (26) The tilted supine position or the use of wedges or cushions for prevention of hypotension has been widely adopted. (14,25,29-31) However, a recent systematic review assessed maternal positions during cesarean section for preventing maternal and neonatal complications in women receiving spinal anesthesia. (8) The review concluded that there is limited evidence to support or disprove the value of tilting, wedges or the use of mechanical displacers. Current evidence suggests that further studies are needed to support this recommendation.

The current study has some methodological limitations. The same anesthetist performed spinal anesthesia, positioned the patient and collected data, and may have introduced bias, limiting the clinical significance of our findings. Neonatal data, both clinical or biochemical, were not collected, and there was no quantification of aortocaval compression or uterine deviation.

In conclusion, in our study population the use of the right lumbar–pelvic wedge, when compared to the complete supine position, was not effective in reducing the incidence of hypotension in spinal anesthesia for cesarean delivery, although vasopressor requirement was significantly decreased. The risk of hypotension in both groups remains substantial.

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SECTION 5

GENERAL DISCUSSION

GENERAL DISCUSSION

This thesis aims to understand important issues on perioperative safety in middle-income countries and provide potential ways to improve quality and safety. This discussion chapter starts with an overview of the findings and considerations of the previous chapters. Then, it presents some perspectives on the ongoing scientific discussions with special emphasis on "evidence" in patient safety, and, finally, it addresses some future developments and areas of interest for further study.

In the last 10 years the author -as anesthesiologist and pain practitioner- has provided perioperative care for many patients. He became conscious of the need to improve quality and safety there and started his research in the field of perioperative safety. Findings presented have contributed mainly to create awareness about potential scenarios to improve quality and safety in the perioperative period in Colombia.

Three major questions were considered as the basic framework of this thesis and this section is directly related to each one: 1) What is the current state of Randomized Controlled Trials and Systematic Reviews on Patient Safety worldwide?, 2) Is there any validated approach to assess safety at perioperative care in middle-income countries like Colombia? and 3) Which perioperative interventions on quality and safety potentially affect patients in low- and middle-income countries?

This thesis

Chapter 1 illustrates that, despite the increased alertness for patient safety, there is still a paucity of evidence about interventions in patient safety -at any level of health care-. Even considering well-ranked journals which address specifically topics related to patient safety and the health-care quality, the number of randomized controlled trials and systematic reviews on patient safety is scarce the limited evidence is mainly from developed high-income countries. In the 37-year period analyzed, there were 83 randomized trials and 64 systematic reviews published (11 with meta-analysis).

Scientific output and evidence in the field of patient safety has increased dramatically in recent years. Much of this consists of basic research in related disciplines such as psychology, sociology or organizational studies (1,2). However, none of the top 10 highest-cited patient safety papers comes from a low- or middle-income country (2).

Research on the efficacy of the interventions to decrease unnecessary risks related with patient safety has some particularities, clarified by Brown et al.: First, patient safety interventions are often "complex interventions" which require a carefully planned evaluation and development. Sometimes interventions as well as outcome evaluations are difficult to blind. Second, patient safety interventions are often delivered and implemented at "groups of subjects" (or clusters, i.e. people at operating room, hospitals, certain population area) rather than at an individual level, in an equally complex environment, such as

health organizations. Third, patient safety interventions are often expected to do more good than harm, implying that professional equipoise may be absent. Therefore, traditional study designs such as a parallel randomized controlled trial may not be ethically acceptable. Finally, if patient safety research refers to interventions to prevent harm, countable outcomes are rare events and in many times difficult to assess. They entail for large multicenter studies and collaboration with increase in cost and logistics (1,3–6).

Prospective randomized controlled trial is considered the research design of choice to evaluate the efficacy of health interventions providing the most robust evidence (7). Nevertheless, interventions in patient safety are not suitable to be studied using only this approach. Clearly, studies on interventions (using randomization) are less common than large observational population studies into the incidence and causes of medical errors (2). At a first glance, this could be interpreted as a lack of strong evidence, but as Leape et al. suggest this lack of evidence means that "the traditional evidence-based approach cannot be the sole source of information for advancing patient safety" (5,8).

In quality and patient safety, improvement initiatives could be practical (aimed at producing change) and scientific (aimed at producing new knowledge). These initiatives include more methodological and study designs approaches like variants of trial designs, stepped wedge trial designs, quasi-experimental designs, before-after studies, program evaluations, process evaluations, qualitative studies and economic evaluations (9).

A limitation of chapter 1 is that it does not provide an overall overview of all those approaches. Nevertheless, randomized studies included in this chapter addressed important patient safety topics, like clinical process or procedures, resources or organizational management, medical devices and equipment and finally, safety during the administration of medication or intravenous fluids. Many of them have direct relationship with the perioperative period. In 2004, the World Alliance for Patient Safety of the World Health Organization launched a consensus-based list of global priorities for patient safety, including a research agenda (10,11). After its first edition, this list has not (yet) been updated. The work presented in chapter 1 showed the very limited number of randomized trials and systematic reviews published on the effect of interventions to improve hot listed topics by the World Health Organization. This may reflect an undetermined number of randomized trials and systematic reviews that are published in journals of general practice or other medical specialties due to their special scope (2).

Finally, chapter 1 shows how it is still necessary to hand-search in deep to discover interventions related to patient safety published in the literature. This finding is in agreement with those of other authors who state that hand-search in combination with an electronic search is still the most comprehensive approach to overcome limitations of an electronic process and to reduce retrieval bias (12,13).

Culture assessment tools provide an understanding to develop an action plan to improve patient safety (14). The Hospital Survey on Patient Safety Culture was designed to assess staff views on patient safety culture in a hospital and has been translated and validated into several languages and scenarios (15–21). Chapter 2 shows that methods of assessment of safety climate need to be adjusted to regional and local level to meet minimum psychometric criteria. After translation to Spanish and validation process at the perioperative setting, psychometric analyses provided overall support for 9 of the 12 initial factors of patient safety culture and 36 of the 42 initial questions of the questionnaire. Compared to the original version, small shifts of some questions were noted across factors, two factor's titles were modified, and six questions were excluded. These changes could be explained by underlying differences with the original language, cultural environment, and specific setting of use of the questionnaire. The importance of some items that describe interaction among units and teamwork across units may be less perceived in the perioperative setting.

Safety culture is fundamentally a local problem, in that wide variations in the perception of safety culture can exist even within a single organization: the perception of safety culture might be high in one unit within a hospital and low in another unit, or high among management and low among anesthesiologists (22,23). The results of chapter 2 are consistent with previous studies worldwide supporting that questionnaires to asses safety culture require adaptation (including appropriate translation) and setting adjustments (16,18,19,24). Minor differences in this instrument compared with the original one might be not only due to language differences but also due to the setting of use, but this remains as a hypothesis for further studies. This chapter provides the first validated tool for assessment of safety for Latin America, specifically for perioperative settings. Hereby, it aims to stimulate, its broader introduction to the clinical practice in this part of the world considering that it is important to first measure and analyze culture before we can transform it.

Chapter 3 and 4 describe the perceptions of practitioners about quality and safety in relation with a common procedure in perioperative care: central venous catheterization. Chapter 3 is a nationwide survey of registered anesthesiologist at the Colombian Society of Anesthesiologist and showed that ultrasound guidance is not a common technique used for central venous catheterization by Colombian anesthesiologists despite existing evidence that its use enhances safety (25). Interestingly, proportions of use reported in the literature vary between 15% and 96%, depending on the population, year of the survey, country and other hospital settings (26–28). In general, our findings suggests that current use of ultrasound during central venous catheterization in Colombia is not in line with existing evidence-based recommendations. However, this was also seen in developed high-income countries (26–29).

Major barriers for ultrasound guidance use are the lack of equipment and lack of training. Many hospitals in Colombia have only one single portable ultrasound device available in many services and wards. Therefore, knowing that the equipment is available at the hospital does not guarantee its use all the time. In addition, lack of training remains a limitation. The association between age and use of ultrasound for central venous catheterization disappears after adjustment for potential confounders, including availability of the equipment. The low reported use of ultrasound guidance may even be an optimistic estimate, given that some reporting and response bias likely existed in that respondents at certain age, or those using ultrasound guidance could have been more motivated to complete the questionnaire - in which case the frequency of use would be overestimated. Other potential reasons for not using ultrasound guidance may include time pressure and "individual perceptions" about experience, expertise, effectiveness and patient care.

In agreement with results of chapter 3, Henwood et al. recently conducted a nationwide survey of Colombian emergency medicine residents indicating the lack of instructors, equipment and time as a major restrictions to use ultrasound during central venous catheterization (30). These findings, could probably apply to other specializations in Colombia, as well as for other low- or middle-income countries. Fortunately, most anesthesiology residency programs in Colombia now include ultrasound imaging in their medical education, training and clinical practice.

Chapter 4 shows that the use of a landmark technique for catheterization suffers from evident safety issues due to potentially preventable complications. In this study, estimated incidence of mechanical complications was 17%. Similar figures have been previously described, but almost exclusively from high-income country settings, which implies that the incidence of complications is similar for high and middle-income countries.

The number of (attempted) punctures was strongly associated with mechanical complications. The increase in the odds ratio with each of the following puncture compared with the previous one is 1.9. Mansfield et al. described how the rate of complications increases with more than 2 passes of the needle and Eisen et al. showed an odds ratio for mechanical complications of 3.6 with more than 2 punctures (31,32). Findings of chapter 4 are consistent with previous studies and confirm the importance of the number of punctures and mechanical complications during central venous catheterization. Additionally, chapter 4 demonstrates that the increased odds ratio with more punctures in comparison with one has a slow rise until 3 punctures after which it becomes exponentially. Therefore, we support the recommendation not to perform more than 3 punctures at the same site.

Chapters 5 and 6 are related to anesthesiological care of obstetric patients. First, after a Cochrane systematic review it was interesting to discover that in patients with

an incomplete miscarriage undergoing evacuation, there is not one unique anesthetic technique to choose. Particular considerations that influence the choice of anesthesia technique for this procedure such as availability, effectiveness, safety, side effects, practitioner's choice, costs and woman's preferences of each technique should be applied when making clinical choices.

Chapter 5 systematically reviewed seven randomized controlled trials involving a total of 800 women comparing effects of any anesthetic technique (general anesthesia, sedation/analgesia, regional or paracervical block) for evacuations of incomplete miscarriages. The available literature remains scarce and suffers from moderate to high risks of bias. In addition, high heterogeneity of interventions and reported outcomes prevents statistical pooling and meta-analysis. In terms of postoperative pain, paracervical block does not improve the control of postoperative pain when compared to sedation/analgesia or versus no anesthesia/no analgesia. The addition of lidocaine to paracervical block versus saline provides better control of postoperative pain. When opioids were used, postoperative nausea and vomiting were more frequent in two trials compared with those using paracervical block. Since 2012, new studies were published considering paracervical block and/or sedation for patients undergoing evacuation of an incomplete miscarriage (33,34) and these findings should be included in an update of the systematic review presented in the chapter 5 of this thesis.

Lack of high-quality evidence is a relative common scenario in anesthesia and evidence based medicine. Clinicians should combine the use of the best-available evidence with their pathophysiological knowledge taking into account mainly, the preferences of patients after a detailed discussion in order to provide the best and safest care (35).

Finally, chapter 6 evaluated the effectiveness of a mechanical low-cost intervention using a right lumbar-pelvic wedge in preventing hypotension after spinal anesthesia for cesarean delivery, a common scenario in low- and middle-income countries. It is ubiquitous obstetric anesthesia practice to implement left lateral uterine displacement in all women during cesarean delivery following the recommendations of several clinical practice guidelines (36,37). In this randomized trial, the use of this intervention was not effective in reducing the incidence of hypotension during spinal anesthesia for cesarean section.

The real value of patient positioning during cesarean section has been under scrutiny, as well as, the existence or clinical relevance of the aortocaval compression syndrome (38). Recent evidence using magnetic resonance images in term singleton pregnant women, confirms that the aorta at the mid- to upper lumbar disk levels was not compressed by using left-lateral tilt and the inferior vena cava is relieved only at a tilt of 30° but not at 15° (39). A Cochrane systematic review assessed maternal positions during cesarean section under spinal anesthesia for preventing maternal and neonatal complications and concluded that there is limited evidence to support or disprove the value of

tilting, wedges or the use of mechanical displacers (40). During the last updating of this review, the paper (contents of chapter 6) was included in order to reduce uncertainty about this intervention without changing the main conclusions.

The incidence of hypotension varies according to its definition and limits comparability of different preventive measures (41,42). Chapter 6 used a commonly accepted definition, and the incidence was high but in agreement with other studies (43). Single blinding and no collection of neonatal data, both clinical or biochemical, were important limitations of this randomized controlled trial. Recent studies suggest that when maternal systolic blood pressure was maintained with fluid and phenylephrine, there was no apparent benefit to left lateral uterine displacement on hemodynamics as well as on neonatal acid-base status during cesarean delivery (38,44,45). Therefore, positioning strategies and recommendations from current guidelines for women undergoing (elective) cesarean section could be refined.

Ongoing scientific discussions

Perioperative safety needs to be contextualized and this thesis provides a validated tool for assessment, specifically for perioperative settings in Colombia. Researchers should try to explore more operating rooms at national level and in other Latin American countries, in order to discover trends, differences and major concerns about safety. In addition, such studies would add more evidence regarding the psychometric properties of the Hospital Survey on Patient Safety Culture questionnaire in the perioperative setting. Similarities between countries (and cultures) would suggest that the questionnaire could be used interchangeably or with minor adjustments (15,18,19,21,46). It more widespread use could answer questions like: Is the current Colombian (at Popayán city) validation appropriate for other cities in Colombia or even other Latin American countries? Are there differences in cultural environment affecting the validity of the questionnaire in Latin-America?.

At the moment, there are no clear strategies to expand the use of ultrasound guidance during central venous catheterization in Colombia. Due to the restricted availability, which is mostly due to financial shortages, its use is low and the perception about quality and safety does not seems to affect the current practice. With the estimated costs of a basic ultrasound equipment being around 50.000 USD, this remains as a problem of potential improvement.

Increase in the amount of studies available in the scientific medical literature is very fast and expanding exponentially. The information provided in Chapters 1 and 5 should be updated to add more recent evidence to their questions. How much of these new data is coming from low- or middle-income countries, any from Latin America? Is patient safety in the perioperative setting receiving more attention in recent years? In this re-

gard, low- and middle-income countries need to produce more high-standard evidence in quality and safety in the perioperative setting.

Some issues suggest strong similarities between countries but there is scarcity of information to contrast. Therefore, there is a patient-safety paradox in scientific literature: developed high-income countries with a high safety level produce the most available literature, whilst evidence from low- and middle-income countries which would have a much bigger benefit is lacking. While research agenda in patient safety may prioritize some concerns to certain countries or areas, there are many common issues that could be addressed globally with collaboration.

"Evidence" and patient safety

From its origins in 1990s, evidence based medicine was a movement supporting the use of evidence from high-quality randomized controlled trials and observational studies, in combination with clinical expertise and the needs and wishes of patients (35). Evidence based medicine quickly became a core topic in an intellectual community committed to making clinical practice more scientifically and empirically grounded and thereby achieving safer, more consistent, and more cost effective health care (47,48).

Taking into account that not all situations in health care require nor enable a randomized controlled trial, nobody denies the advantages of this movement and its successes (47,49,50). Sometimes, high-quality evidence could not be available and in addition, evidence could be biased by vested interests to favor some actors of the process, e.g. industry or opinion leaders (47,51,52). Much of the work of evidence based medicine has focused on issues of "evidence", i.e. the problems of bias and error, the use of composite endpoints, the abuse of surrogate markers and subgroup analyses, selective dissemination of evidence and limited translation and implementation to real clinical scenarios (53).

Clinical practice must survive and improve in this "non-perfect world". To apply "evidence" in the clinical care of an individual patient, clinical expertise becomes very important. Clinical expertise includes the combination of physiology, pathology, pharmacology, and many other information with clinical experience into practice (54) and balancing them using critical thinking for decision-making. "Critical thinking" focuses on asking appropriate questions allowing to examine existing concepts, beliefs and biases for the purpose of enhancing and improving understanding and problem-solving (55). This mind-set, that dates back to the days of Socrates (470-399 BC), should not be confused with "educated guessing". Then, by "critical thinking", clinicians are able to decide if evidence fits with the concrete, individual circumstances and apply it. That way, evidence based medicine does not become a law, but a scientifically well-based recommendation.

Evidence based medicine must be understood as a combination of scientific tools developed to improve patient care. Therefore, evidence based medicine should not be

about "evidence", but about responding to patient problems -as much as possible- with evidence. In order to judiciously adapt "evidence" to the care of individual patients -in their particular situations- it is necessary to know how patients think and feel about their problems (52). Clinicians cannot discover patient values, preferences, and contexts without interacting meaningfully with them and researchers have been including more and more patient-reported outcomes in order to meet a common road for "evidence" and patient preferences and concerns. This way, evidence based medicine enables both: shared-decision making between care-provider and patient based on evidence based data and value-based health-care taking into account, that the patients can finally experience the potential benefits of their surgical intervention.

Finally, evidence based health care must integrate patient safety, too. As other areas, patient safety can be refined by using high-quality evidence, but considering its particularities and differences. Observational data are highly relevant in patient safety research and sometimes considered enough to implement policies, as well as, common sense interventions. In addition, it is unrealistic to wait for randomized controlled studies for all interventions in patient safety. A great approach to integrate evidence based medicine principles in patient safety was described by Kaveh Shojania et al. and Lucian Leape et al. in 2002: "the best approach for ensuring patient safety will be one in which the general insistence on evidence does not prevent implementation of practical, low-risk, -but understudied- interventions, that rationally seem likely to work" (8,56). Hereby they clearly state, that evidence based medicine includes "critical thinking".

Future perspectives

In the previous years, there had been incredible innovations in anesthesia, such as the introduction of new anesthetics, new devices for airway management and advanced monitoring of vital signs. The developments from recent years reflect the maturity of anesthesia as a specialty with a steadily decline in perioperative mortality (57,58). To enable healthcare professionals to adapt themselves to all these changes, continuous medical education must be prioritized. Training does not stop after medical residency training and we should be very aware about that. Colombian Society of Anesthesiologist (SCARE) is leading the process of re-certification in Colombia for the specialty, but the government should pursue policies towards efficient and effective continuing medical education for all specialties (59,60).

Nowadays, clinical and scientific work is focused on continuous improvement, a better understanding of patient outcomes, and delivery of the highest quality of care through education and training, research, audit, incident reporting, and the setting of safety standards (61). Quality and patient safety are integral part of high-quality patient care and they must be considered as undistinguishable.

Our primary mission in health care is to improve the health and quality of life of patients. This begins with a properly understanding about what do they recognize as quality of life, what do they report and to what do they give more importance. Value-based health care requires patients to provide information regarding their feelings, their symptoms and any short- or long-term effect of health interventions. Patient reported outcomes seem to be more important than any other outcomes like clinical, physiological, biochemical or caregiver-reported (62–64). In perioperative care, patient reported outcomes measures (PROMs) and patient reported experience measures (PREMs) are the missing link in defining a good outcome and much of the current research should consider to implement these type of measures to address real quality of care (65). Potential areas of research include short- and long-term patient important outcomes in perioperative care, effects of perioperative interventions on quality of life afterwards and to look for more appropriate metrics to measure the contribution of anesthesiology -as a part of a perioperative system- in the total quality of care and patient experience (66).

In terms of safety culture, potential areas of improvement for low- and middle-income countries are: 1) implementation of non-blaming systems to report adverse events, 2) enhancement of non-punitive policies with respect to error reporting, 3) promotion of open communication, and 4) promotion of management support of safety culture, including assessment (67) (Figure 1).

Figure 1. Strategies to promote improvements in safety at perioperative period focused of the evaluation and response to error.

Anesthesiology has been acknowledged as the leading medical specialty in addressing issues of patient safety at perioperative period, but also, should pursue to impact outside of operating rooms (68). Almost all mechanisms described on this thesis are related mainly with a micro-level framework (Patient centered care by providers) in healthcare, and some of them on the meso-level (Hospital strategies and processes) (57). Colombia, as well as similar countries, has an interesting diversity of healthcare needs. In urban settings, the healthcare offer is among the best in Latin America with top-quality hospitals and educational programs comparable to those in the US or Europe. In contrast, in most rural areas, including some of the most remote locations in the world (like the pacific coast or the Amazon forest), a frail and fragmented healthcare system prevails, similar to those in third world countries (69–71). This diversity, represents a strong challenge for patient safety because measures and interventions would be adapted depending on the level of care pretending to improve. How to deal with such a strong diversity in many aspects at the same time? Additionally it is important to understand how macro-level related major external factors that influence clinical performance such as economic and administrative issues, social conditions, technological changes and health care inequities influence quality of care in general and patient safety in particular (72–74).

Based on the findings presented in this thesis and during its development, some measures have been adopted by practitioners, managers and academics at Universidad del Cauca, Hospital Universitario San José and Clínica La Estancia, all in Popayán, Colombia in benefit of quality and safety of patients during the perioperative period. During the development of this thesis, the author has made a strong and long-standing collaborative relation with the Department of Anesthesiology of Erasmus University Medical Center involving many members of the Departamento de Anestesiología of the Universidad del Cauca. This demonstrates the direct impact of research-based collaborative efforts between countries (75).

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SUMMARY

This thesis aims to understand important issues on perioperative safety in middle-income countries. It starts with an **introduction** which addresses the state of perioperative patient safety, then it provides some broad ideas about patient safety culture and lastly, it addresses specific measures and interventions to improve quality and safety.

Based on this background and the findings of this thesis, 3 key-questions are discussed:

Question 1: What is the current state of Randomized Controlled Trials and Systematic Reviews on Patient Safety worldwide?

Chapter 1 states that even with the current worldwide awareness on quality and safety, there is still a paucity of evidence about interventions aimed to improve patient safety, at any level of healthcare. The number of randomized controlled trials and systematic reviews on patient safety is scarce and coming mainly from high-income countries. In the 37-year period analyzed, there were 83 randomized trials and 64 systematic reviews published. The first randomized controlled trial was published in 1992, the period from 2003 to 2007 had the highest number of publications and 30% of the total were published protocols. Allocation to interventions at the group level (randomization performed by clusters) was reported in 34% of trials and most approached complex interventions. Furthermore, included studies addressed important topics, some strongly related with interventions in the perioperative period, i.e. safety during the administration of medication or intravenous fluids, resources or organizational management and medical devices and equipment. Also, chapter 1 shows how it is still necessary to combine electronic searches with hand-search in deep, in order to discover literature about interventions on patient safety published in the literature.

Question 2: Is there any validated approach to assess safety at perioperative care in middle-income countries like Colombia?

Chapter 2 presents a Spanish translation, validation and adaptation to perioperative settings in Colombia of The Hospital Survey on Patient Safety Culture questionnaire. Psychometric analyses provided overall support for 9 of the 12 initial factors of patient safety culture and 36 of the 42 initial questions of the questionnaire. Compared to the original version, small shifts of some questions were noted across factors and two factor's titles were modified to increase their understanding. The importance of some questions that describe interaction among units and teamwork across units may be less perceived in the perioperative setting. All changes made could be explained by underlying differences with the original language, cultural environment, and specific setting of use of the questionnaire. Chapter 2 shows that methods of assessment of patient safety culture need to be adjusted to regional and local level to meet minimum psychometric criteria.

Also, this chapter provides the first validated tool for assessment of patient safety for Latin America, specifically for surgical settings.

Question 3: Which perioperative interventions on quality and safety potentially affect patients in low- and middle-income countries?

Chapter 3 and **Chapter 4** describe the perceptions of practitioners about safety in relation with a common procedure in anesthesia and intensive care medicine: central venous catheterization. A nationwide Colombian survey showed that ultrasound guidance during catheterization is not a common technique used by anesthesiologists. Less than 50% of the colleagues reported to use it at least sometimes or always, despite existing evidence that its use enhances safety. Among users, most obtained training through external courses or from colleagues. Lack of ultrasound equipment available at all time was independently associated with the non-use of ultrasound during central venous catheterization.

In contrast, Chapter 4 estimates an incidence of 17 % of mechanical complications after central venous catheterization using the classical landmark technique. The number of attempts was strongly associated with mechanical complications and the increase in the odds ratio with each of the following puncture compared with the previous one was 1.9. Additionally, chapter 4 demonstrates that the increased odds ratio for complications with more punctures in comparison with one has a slow rise until 3 attempts after which it becomes exponential. Our results support the recommendation not to perform more than 3 punctures at the same site. Findings are consistent with previous studies and confirm the importance of the number of punctures for the risk of mechanical complications during central venous catheterization.

Chapters 5 and **Chapter 6** refer to the anesthesiological care of obstetric patients. Chapter 5 systematically reviewed seven randomized controlled trials involving a total of 800 women comparing effects of any anesthetic technique (general anesthesia, sedation/analgesia, regional or paracervical block) in patients with an incomplete miscarriage undergoing surgical evacuation. The available literature remains scarce and suffers from moderate to high risks of bias. In addition, high heterogeneity of interventions and reported outcomes prevents statistical pooling. In terms of postoperative pain, paracervical block does not improve the control of postoperative pain when compared to sedation/analgesia or versus no anesthesia/no analgesia. The addition of lidocaine to paracervical block versus saline provides better control of postoperative pain. When opioids were used, postoperative nausea and vomiting were more frequent in two trials compared with those using paracervical block. Search did not find any trial reporting data about maternal mortality and two trials showed conflicting results in terms of requirement of blood transfusion. There is not one unique anesthetic technique to choose. Particular considerations such as availability, effectiveness, safety, side effects,

practitioner's choice, costs and woman's preferences of each technique should be applied when making clinical choices.

Finally, chapter 6 evaluated the effectiveness of a mechanical intervention using a right lumbar-pelvic wedge in preventing hypotension after spinal anesthesia for elective cesarean delivery. In this randomized clinical trial, eighty healthy women were randomly allocated immediately after spinal blockade to either a lumbar-pelvic wedge positioned under the right posterior-superior iliac crest or the complete supine position and hypotension was defined as a reduction in systolic blood pressure of 25% from baseline. The use of this intervention was not effective in reducing the incidence of hypotension during spinal anesthesia for cesarean section while the risk of hypotension remained substantial in both groups (42.5% versus 50%). However, less vasopressor's requirement was noted in patients assigned to the lumbar-pelvic wedge group.

In the final **general discussion**, we review the findings of the papers presented, ongoing scientific discussion and address future perspectives in the context of low- and middle-income countries.

SAMENVATTING

Dit proefschrift heeft als doel de belangrijke problemen rondom perioperatieve veiligheid in landen met een gemiddeld inkomen te begrijpen. Het begint met een **inleiding** over de globale toestand van perioperatieve patiëntveiligheid in deze landen. Vervolgens behandelt het een aantal uiteenlopende ideeën over het veiligheidsklimaat en meting hiervan, en ten slotte werpt het een blik op specifieke en regionaal aangepaste interventies om de veiligheid van patiënten te verbeteren.

Op basis van deze achtergrond worden 3 kernvragen behandeld in dit proefschrift:

Vraag 1: Wat is de huidige status van gerandomiseerde onderzoeken en systematic reviews over patiëntveiligheid wereldwijd?

Hoofdstuk 1 stelt dat zelfs met de huidige ontwikkeling op het gebied van patiëntveiligheid, er nog steeds een gebrek aan bewijs is over interventies hieromtrent - op elk niveau van gezondheidszorg. Het aantal gerandomiseerde onderzoeken en systematic reviews over patiëntveiligheid is schaars en komt voornamelijk uit ontwikkelde landen. Over een periode van 37 jaar zijn er 83 gerandomiseerde studies en 64 systematic reviews over dit onderwerp verschenen. De eerste gerandomiseerde studie dateert uit 1992. Tussen 2003 en 2007 ziet men een publicatiepiek, waarvan 30% protocollair is en 34% (vaak hoog complexe) interventies onderzocht middels cluster randomisatie. De overige studies hebben betrekking op andere belangrijke onderwerpen, zoals klinisch processen of procedures, middelen (kennis) of organisatiebeheer, medische hulpmiddelen en apparatuur en veiligheid tijdens de toediening van medicatie of IV-vloeistoffen. Veel van deze elementen hebben een directe relatie tot het perioperatieve niveau. Tot slot laat hoofdstuk 1 zien dat het nog steeds nodig is grondig en gedetailleerd te zoeken in de literatuur naar publicaties over interventies met betrekking tot patiëntveiligheid.

Vraag 2: Bestaat er een gevalideerde aanpak om de veiligheid op perioperatief niveau te beoordelen in ontwikkelingslanden zoals Colombia?

In hoofdstuk 2 wordt een Spaanstalige versie van de 'Hospital Survey on Patient Safety Culture' gepresenteerd, inclusief validatie en adaptatie naar de perioperatieve setting in Colombia. Van de originele vragenlijst zijn op het gebied van patiëntveiligheid 9 van de 12 factoren, en 36 van de in totaal 42 vragen overgenomen. Sommige vragen zijn aangepast om deze begrijpelijker te maken. Het werd duidelijk dat sommige meetmethoden over interacties binnen èn tussen verschillende afdelingen van een ziekenhuis niet altijd even goed begrepen worden. De gemaakte aanpassingen zijn te verklaren aan de hand van taalbarrières, cultuur, lokale gebruiken en omstandigheden waarin de vragenlijst werd gebruikt. Dit hoofdstuk laat zien dat de meetmethoden voor een veilig ziekenhuisklimaat moeten worden aangepast aan het regionale en lokale niveau om

aan minimale psychometrische criteria te voldoen. Verschillen in cultuur, taal en gebruik bepalen hoe - op perioperatief niveau - een meetinstrument kan worden verbeterd. Dit artikel biedt het eerste gevalideerde meetinstrument voor het beoordelen van de veiligheid in Latijns-Amerika en is met name geschikt voor chirurgische instellingen en afdelingen. Het doel is om implementatie in de klinische praktijk in dit deel van de wereld te stimuleren.

Vraag 3: Welke anesthesiologische interventies op kwaliteit en veiligheid kunnen mogelijk van invloed zijn op patiënten in ontwikkelingslanden?

Hoofdstuk 3 en **Hoofdstuk 4** beschrijven de kijk van artsen op veiligheid in relatie tot een algemene procedure bij anesthesie en intensive care: de centrale veneuze katheterisatie. Uit landelijk onderzoek bleek dat echografisch geleid puncteren niet een gangbare techniek is voor Colombiaanse anesthesiologen. Slechts 50% van de respondenten gaf aan hier wel eens gebruik van te maken, ondanks het bewijs dat dit de veiligheid ten goede komt. De belangrijkste belemmeringen voor het verrichten van echogeleide puncties blijken voornamelijk het gebrek aan materiaal, kennis en training te zijn, waarbij het gebrek aan materiaal een onafhankelijk geassocieerd blijkt te zijn.

Hoofdstuk 4 laat zien dat het gebruik van anatomische landmarks, de klassieke benadering, tijdens katheterisatie gepaard gaat met veiligheidsrisico's en dientengevolge resulteren in complicaties die mogelijk te voorkomen zijn. De incidentie van procedure gerelateerde complicaties was 17% en nam toe met het aantal uitgevoerde pogingen met een odds ratio van 1,9. Het keerpunt lijkt bij 3 pogingen te liggen: de kans op complicaties stijgt hierna exponentieel. Deze resultaten onderschrijven de volgende aanbevelingen: beperking van het aantal pogingen tot maximaal 3 keer op dezelfde plek, gepaste supervisie en het gebruik van ultrasone begeleiding.

Hoofdstukken 5 en **Hoofdstuk 6** hebben betrekking op anesthesiologische zorg voor gynaecologische patiënten. In hoofdstuk 5 wordt een systematic review gepresenteerd waar in totaal zeven onderzoeken worden behandeld met in totaal 800 vrouwen. De effecten van verschillende typen anesthesie (algeheel, sedatie analgesie, regionaal of paracervicaal blok) worden met elkaar vergeleken.

Er is geen "standaard anesthesie" bij evacuatie van een onvolledige miskraam en er is maar weinig over bekend in de literatuur. Door de grote verscheidenheid aan interventies en gerapporteerde uitkomsten is het niet eenvoudig de resultaten te poolen. Ter bestrijding van postoperatieve pijn bleek een paracervicaal blok niet superieur te zijn aan sedatie analgesie noch een conservatief beleid. Toevoeging van lidocaïne aan een paracervicaal blok bleek echter wel superieur wanneer vergeleken met een fysiologische zoutoplossing. Twee onderzoeken toonden aan dat het gebruik van opioïden leidde tot meer postoperatieve misselijkheid en braken wanneer vergeleken met een paracervicaal blok. De gebruikte zoekstrategie leverde geen resultaten op over artikelen

die maternale sterfte beschrijven. Twee artikelen lieten tegenstrijdige resultaten zien op het gebied van (al dan niet noodzakelijke) bloedtransfusies. Concluderend wordt gesteld dat bepaalde overwegingen die van invloed zijn op de keuze van de anesthesie voor deze procedure, zoals beschikbaarheid, effectiviteit, veiligheid, bijwerkingen, keuze van de behandelaar, kosten en voorkeuren van vrouwen van elke techniek, zullen telkens opnieuw moeten worden afgewogen.

Tot slot gaat hoofdstuk 6 over het gebruik van een wedge ter voorkoming van de compressie van de vena cava tijdens een linker baarmoederverplaatsing. In dit artikel worden 80 gezonde vrouwen gerandomiseerd op behandeling met wedge, geplaatst onder de rechter spina illiaca superior posterior, of zonder wedge in rugligging. Hypotensie was gedefinieerd als een bloeddruk verlaging van 25% of meer ten opzichte van de uitgangswaarde bij aanvang van de operatie. De incidentie van maternale hypotensie verbeterde niet bij patiënten die een keizersnede met spinale anesthesie ondergaan: het risico op hypotensie bleef substantieel voor beide groepen: 42.5% versus 50% respectivelijk. Echter, er bleek minder vasopressie te worden gebruikt in de wedge groep.

In de algemene **discussie** bekijken we de bevindingen van de gepresenteerde artikelen en bespreken we toekomstige perspectieven in de context van ontwikkelingslanden.

RESUMEN

Esta tesis busca comprender temas relevantes sobre seguridad perioperatoria en países de ingresos medios. Inicia con una **introducción** que aborda el estado global y regional de la seguridad perioperatoria del paciente, luego brinda algunas ideas generales sobre la cultura de seguridad y por último, aborda algunas medidas e intervenciones específicas para mejorar la calidad y la seguridad.

Basándose en estos antecedentes, se abordan 3 preguntas claves para resumir los hallazgos presentados:

Pregunta 1: ¿Cuál es el estado actual de los ensayos controlados aleatorios y las revisiones sistemáticas sobre la seguridad del paciente en todo el mundo?.

El **Capítulo 1** establece que incluso con la actual conciencia mundial sobre la calidad y la seguridad de la atención en salud, todavía hay escasez de evidencia sobre intervenciones destinadas a mejorar la seguridad del paciente, en cualquier nivel de atención médica. El número de ensayos controlados aleatorios y revisiones sistemáticas sobre seguridad del paciente es escaso y proviene principalmente de países de ingresos elevados. Se analizó un periodo de 37 años en el cual se publicaron 83 ensayos aleatorios y 64 revisiones sistemáticas. El primer ensayo controlado aleatorio se publicó en 1992. El período de 2003 a 2007 presentó el mayor número de publicaciones y el 30% del total fueron protocolos publicados. La asignación de intervenciones en grupos (*clusters*) fue reportada en 34% de los ensayos y la mayoría de las intervenciones se clasificaron como complejas. Los estudios incluidos abordaron temas importantes, algunos fuertemente relacionados con intervenciones en el período perioperatorio. Entre ellos tópicos de seguridad durante la administración de medicamentos o líquidos intravenosos, recursos y gestión organizativa, y gestión de dispositivos y equipos médicos. Adicionalmente, el capítulo 1 muestra cómo todavía es necesario combinar las búsquedas electrónicas con búsqueda manual en profundidad para localizar literatura publicada sobre intervenciones en seguridad del paciente.

Pregunta 2: ¿Existe alguna herramienta validada para evaluar la seguridad del paciente a nivel perioperatorio en países en desarrollo como Colombia?.

El **Capítulo 2** presenta una traducción, validación y adaptación al entorno perioperatorio en Colombia del cuestionario *Hospital Survey on Patient Safety Culture*. El análisis psicométrico apoyó 9 de los 12 factores iniciales de la cultura de seguridad del paciente y 36 de las 42 preguntas originales del cuestionario. En comparación con la versión original, se observaron pequeños cambios de algunas preguntas entre los factores y se modificaron los títulos de dos factores para aumentar su comprensión. La importancia de algunas preguntas que describen la interacción entre unidades hospitalarias y el trabajo en equipo entre unidades puede percibirse menos relevante en el entorno perioperatorio. Todos los cambios realizados podrían explicarse por las diferencias subyacentes con

el idioma original, el entorno cultural y el ambiente de uso del cuestionario. El Capítulo 2 muestra que los métodos para evaluación de la cultura de seguridad del paciente deben ajustarse a nivel regional y local para cumplir con mínimos criterios psicométricos. Además, este capítulo proporciona la primera herramienta validada para la evaluación de la seguridad del paciente en América Latina, específicamente para entornos quirúrgicos.

Pregunta 3: ¿Qué intervenciones anestésicas sobre la calidad y la seguridad pueden afectar a los pacientes en los países de ingresos bajos y medios?.

El **Capítulo 3** y el **Capítulo 4** describen las percepciones médicas sobre seguridad en relación con un procedimiento común en anestesiología y cuidados intensivos: la cateterización venosa central. Una encuesta colombiana en anestesiólogos muestra que el uso de ultrasonido como guía del procedimiento es infrecuente. A pesar de la evidencia existente de que su uso mejora la seguridad del procedimiento, menos del 50% de los especialistas reportaron usarlo al menos a veces o siempre durante la cateterización. Entre los usuarios del ultrasonido, el entrenamiento y formación fueron obtenidos a través de cursos externos o de colegas. La ausencia de un equipo de ultrasonido disponible en todo momento se asoció de forma independiente con la no utilización del mismo durante el cateterismo venoso central.

En contraste, el **Capítulo 4** estimó una incidencia de 17% de complicaciones mecánicas después de la cateterización venosa central utilizando la técnica clásica guiada por estructuras anatómicas. El número de intentos estuvo fuertemente asociado con la presencia de complicaciones mecánicas y el incremento en la razón de probabilidades (*odds ratio)* con cada punción comparada con la anterior fue de 1.9. Adicionalmente, el capítulo 4 demuestra que hay un incremento exponencial de la razón de probabilidades para complicaciones mecánicas después de 3 punciones en comparación a una única punción. Nuestros resultados respaldan la recomendación de no realizar más de 3 punciones en el mismo sitio anatómico. Los hallazgos son consistentes con estudios previos y confirman la importancia del número de punciones en el riesgo de complicaciones mecánicas durante la cateterización venosa central.

El **Capítulo 5** y el **Capítulo 6** se refieren a la atención anestésica de pacientes obstétricas. El Capítulo 5 revisó sistemáticamente siete ensayos controlados aleatorios con un total de 800 mujeres que compararon los efectos de cualquier técnica anestésica (anestesia general, sedación/analgesia, bloqueo regional o paracervical) en pacientes con diagnostico de aborto espontáneo incompleto que se sometieron a evacuación quirúrgica. La literatura disponible es escasa y presenta un riesgo de sesgo moderado a altos. Además, la alta heterogeneidad de las intervenciones y los resultados reportados limitan la síntesis estadística. El bloqueo paracervical no mejora el control del dolor postoperatorio en comparación con la sedación/analgesia o versus sin anestesia/sin analgesia. La adición de lidocaína al bloqueo paracervical versus solución salina proporciona un mejor control del dolor posoperatorio. Cuando se usaron opioides, la

náusea y vómito postoperatorio fueron más frecuentes en dos ensayos en comparación con los que usaron bloqueo paracervical. La búsqueda no encontró ningún ensayo que proporcionara datos sobre mortalidad materna y dos ensayos mostraron resultados contradictorios en relación a las necesidades de transfusión sanguínea. En conclusión, no existe una técnica anestésica única para seleccionar. Durante la escogencia, consideraciones particulares como la disponibilidad, eficacia, seguridad, efectos secundarios, elección del médico, costos y principalmente las preferencias de cada paciente respecto de cada técnica deben aplicarse.

Finalmente, el capítulo 6 evaluó la efectividad de una intervención mecánica utilizando una cuña lumbar-pélvica derecha para prevenir la hipotensión después de anestesia espinal para el parto por cesárea electiva. En este ensayo clínico aleatorizado, ochenta mujeres sanas fueron asignadas aleatoriamente inmediatamente después del bloqueo espinal al uso de una cuña lumbar-pélvica colocada debajo de la cresta ilíaca posterior-superior derecha o la posición supina completa. La hipotensión se definió como una reducción en la presión arterial sistólica de un 25 % del valor inicial. El uso de esta intervención no fue eficaz para reducir la incidencia de hipotensión durante la anestesia espinal para la cesárea, mientras que el riesgo de hipotensión siguió siendo importante en ambos grupos (42,5% versus 50%). Sin embargo, se observó una menor necesidad de vasopresores en las pacientes asignadas al grupo de cuña lumbar-pélvica.

En la **discusión general** final, revisamos los hallazgos de los artículos presentados, la discusión científica en curso y abordamos las perspectivas futuras en el contexto de los países de ingresos bajos y medios.

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First, I am very grateful to all the patients and participants included in my research, their contribution is much bigger than they can imagine. Knowledge is constructed by adding small pieces and I really hope these results and this overall thesis may somehow aid in improving patient safety and quality in Colombia and in other countries. Thank you and my respect.

Undertaking PhD studies while in active clinical practice is a remarkable and strong experience. It becomes part of your daily life and part of your way of thinking. It also changes the way you perceive the world and each situation you live is continuously questioned. As a clinician, every time I have evaluated a patient I have to think again critically if my choices are the best I can do. Doing research while I was practicing also made me confront several complex situations with opportunities to improve safety and quality during the perioperative period. I would like to have chosen more but logistics and funding were scarce. Also, it demands great discipline and time-management. Clinical practice afforded me the opportunity and capacity to raise good clinical questions and choose the most interesting, relevant, and suitable research scenarios. My gratitude goes to all the medical specialists, particularly anesthesiologists, surgeons, and gynecologists at Hospital Universitario San Jose and La Estancia Clinic in Popayán, who, through their own unique contributions, have made it possible to participate in and contribute to medical research. I would also like to acknowledge all my medical residents, nurses, interns, and medical students at Hospital Universitario San José and La Estancia Clinic in Popayán, especially those who contributed to our research.

When I finished my MSc program in 2010, I said some words I probably could not understand properly, but ten years later, they are still valid: "For me, it (this PhD degree) represents much, much more than a degree. It represents a lifestyle and a new way of perceiving my career with criticism and with wishes to go one step forward every day in knowledge." I have no words to express my gratitude to all the people who contributed directly or indirectly to this purpose. In a country like mine, Colombia, and in many other places, many people live with difficulties and search every day for opportunities, like the opportunity granted me. I am really convinced that we just need these opportunities to show our capabilities. I wish to thank the Erasmus-Columbus and ERACOL program for supporting me at the beginning and thank the universe for bringing me to the door of the Anesthesiology department of Erasmus MC that day.

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CURRICULUM VITAE

José Andrés Calvache was born on July 1, 1983 in Puerres-Nariño, Colombia. He attended pre-university education at Concentración Escolar Piloto and Colegio Juan XXIII in Puerres and Colegio San Felipe Neri in Pasto, Colombia and finished in 2000 "with academic excellence". He started medical studies in June 2000 in the Faculty of Health Sciences at Universidad del Cauca in Popayán, Colombia. During the early years of his career, he identified that he wanted to become a clinician-researcher and started his training with early mentorship by Prof. Mario Delgado in clinical and public health research. In 2006, he found interest in anesthesiology and critical care and began working on a research project in the Department of Anesthesiology at Universidad del Cauca, besides projects related with the Clinical Epidemiology Unit and Department of Pediatrics in his Faculty. Along with his medical studies, he attended courses and lectures on data management, web design, and mathematics.

In 2007, he finished his medical studies and received the Universidad del Cauca medal for outstanding academic performance. He began his clinical practice as "rural medical doctor" in the department of Nariño, Colombia, and later as a general practitioner assistant in the Intensive Care Unit at Hospital Infantil Los Angeles in Pasto, Colombia. In 2008, he became resident of Anesthesiology in the Department of Anesthesiology at Universidad del Cauca. During his second year of residency, he received a scholarship funded by the European Union through the Erasmus-Columbus (ERACOL) project, which contacted him with the Netherlands Institute for Health Sciences, NIHES, at Erasmus University Rotterdam, The Netherlands at that time directed by Prof. Albert Hoffman.

In July 2010, he started a Master's Program in Health Sciences, Clinical Epidemiology at NIHES as a member of the Departments of Anesthesiology and Biostatistics and under the supervision of Prof. Robert Jan Stolker and Prof. Emmanuel Lesaffre and with the close support of Dr. Markus Klimek. During his training, José developed and deepened his special interest in clinical epidemiology methods and biostatistics, as well as important topics related with perioperative safety, mainly in middle-income countries. After finishing, he returned to Popayán to finish his residency program and in March 2012, he became a certified anesthesiologist in Colombia.

In 2012, he joined the Department of Anesthesiology at Universidad del Cauca, practicing anesthesiologist in Popayán and maintained close collaboration with the Department of Anesthesiology at Erasmus MC. One year later, he left Colombia again and started a fellowship training on Interventional Pain Management at Recinto de Ciencias Médicas at the University of Puerto Rico, EEUU, where he gained expertise in pain management, palliative care, and interventional techniques. After finishing, he returned to Popayán to work as professor and clinician.

In 2014, he was named Chairman of the Graduate Research Program in the Department of Anesthesiology at Universidad del Cauca. Besides his managerial and clinical activities – mostly as a dedicated pain management medical doctor – José is certified as a clinical professor and research advisor in the Faculty of Health Sciences at Universidad del Cauca and was classified as a senior researcher by Colombia's Administrative Department on Science, Technology, and Innovation, Colciencias.

PHD PORTFOLIO

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COURSES AND CERTIFICATES (SELECTION)

10/18	Certificate course to Editors of Journals. Departamento Administrativo de Ciencia, Tecnología e Innovación (Colciencias). Bogota, Colombia.
10/17	The Ecosystem of Evidence. Evidence based healthcare teachers and developers GIMBE Foundation, Taormina, Italy.
03/17	Applied Statistics and Graphs with R. Universidad del Cauca, Popayán, Colombia.
06/17	Advanced topics in Metanalysis. Universidad Javeriana, Bogotá, Colombia.
06/17	Topics on cancer research. Universidad Javeriana, Bogotá, Colombia.
06/16	Evaluation of Clinical Practice Guidelines. Cochrane Ecuador Meeting. Quito, Ecuador.
08/15	Erasmus Summer Programme. Netherlands Institute for Health Sciences, Rotterdam, The Netherlands.
03/12	15th WFSA World Congress of Anesthesiologists, Buenos Aires, Argentina.

ACTIVITITES AS EDITOR/REVIEWER FOR SCIENTIFIC JOURNALS

Since 2014	Editorial board. Revista de la Facultad de Ciencias de la Salud, Universidad del Cauca, Colombia.
08-18	Invited editor. Colombian Journal of Anesthesiology.
Since 2010	Reviewer for journals, among others: Colombian Journal of Anesthesiology Cochrane Pregnancy and Childbirth Group Journal of Intensive Care Medicine Journal of International Medical Research Saudi Medical Journal Revista del Hospital Infantil de México Revista de la Facultad de Medicina, Universidad Nacional Colombia

LIST OF PUBLICATIONS NOT PRESENTED IN THIS THESIS (SELECTION)

Full details can be consulted at www.jacalvache.com

I. Original articles:

Gómez-Tamayo JC, Puerta-Guarín JI, Rojas-Camejo CM, Caicedo JP, Calvache JA. Inter-rater and intra-rater reliability of the airway diameter measured by sonography. Journal of Ultrasound. 2018;6;21(1):35–40. DOI:http://dx.doi.org/10.1007/s40477-017-0276-z

Quilindo C, Calvache JA, Delgado-Noguera M. Scientific and academic production and visibility of the Faculty of Health Sciences of Universidad del Cauca. Journal of the Faculty of Medicine 2018;66(4):557-563. DOI: http://dx.doi.org/10.15446/revfacmed.v66n4.65208

Delgado AK, Salazar YM, Díaz R, Solano VE, Ruiz G, García MA, Calvache JA. Prognosis of Severe Acute Lower Respiratory Infection in Colombian Children under Five Years of Age. Rev Cienc Salud. 2017;15(3):313-324. DOI:http://dx.doi.org/10.12804/revistas.urosario.edu.co /revsalud/a.6115

Bravo-Peña M, Barona-Fong L, Campo-López J, Arroyave Y, Calvache JA. Assessing the completeness of reporting of observational studies in Colombian Journal of Anesthesiology. Cross sectional study. Rev Colomb Anestesiol. 2017;45:31-8. DOI:10.1016/j.rcae.2016.11.017

Delgado-Noguera MF, Merchán-Galvis AM, Mera-Mamián AY, Muñoz-Manquillo DM, Calvache JA. Evaluación de la calidad metodológica de las Guías Colombianas de Práctica Clínica en Pediatría. Pediatría. 2016:48(4):87-93. DOI: https://doi.org/10.1016/j.rcpe.2015.12.001

Sierra Zúñiga MF, Castro Delgado OE, Merchán-Galvis AM, Caicedo JCC, Calvache JA, Delgado-Noguera M. Factors associated with length of hospital stay in minor and moderate burns at Popayan, Colombia. Analysis of a cohort study. Burns. 2016;42(1):190-195. DOI: 10.1016/j.burns.2015.10.009

Ríos AM, Calvache JA, Gómez JC, Gómez LM, Aguirre OD, Delgado-Noguera MF, Uribe F, Lesaffre E, Klimek M, Stolker RJ. Postoperative laringo-pharyngeal symptoms in elective surgery – Incidence and related factors. Rev Colomb Anestesiol. 2014;42(1):9-15. DOI: 10.1016/j.rcae.2013.10.005

Calvache JA, López H, Castro-Delgado OE. Local experience with caruncular single injection peribulbar anesthesia. Rev Colomb Anestesiol. 2014;42(1):16-9. DOI: 10.1016/j.rca.2013.10.001

Calvache JA, Molina RA, Trochez A, Benitez F, Arroyo L. Percutaneous dilatational tracheostomy without fiber optic bronchoscopy—Evaluation of 80 cases in intensive care. Rev Colomb Anestesiol.2013;41(3):184-9. DOI: 10.1016/j.rcae.2012.07.003

Calvache JA, Sandoval MX, Vargas WA. Pressure applied by the healthcare staff on a cricoid cartilage simulator during Sellick's maneuver in rapid sequence intubation. Rev Colomb Anestesiol. 2013;41(4):261–266. DOI: 10.1016/j.rcae.2013.09.004

Muñoz I, Romero N, Calvache JA. Incidencia de dolor severo post-operatorio en el Hospital Universitario San José de Popayán. Informe preliminar. Revista de la Facultad de Ciencias de la Salud Universidad del Cauca. 2013;15(4):10- 15

Calvache JA, Arroyo L, Molina R, Trochez A, Benitez F, Aguilar L, Molano A, Velásquez G. Características clínicas y desenlaces de pacientes gineco-obstétricas con manejo en cuidados intensivos. Revista de la Facultad de Ciencias de la Salud Universidad del Cauca. 2013;15(1):8-15

Calvache JA, Barajas-Nava L, Sánchez C, Giraldo A, Alarcón JD, Delgado-Noguera M. Risk of bias assessment of clinical trials published in the Revista Colombiana de Anestesiología. Rev Colomb Anestesiol. 2012;40:183-91. DOI: 10.1016/j.rcae.2012.06.009

Calvache JA, Zafra JC. Epidural analgesia during labor. IATREIA . 2008;21(4):355-363.

Arboleda RA, Ausenon AF, Ayala JA, Cabezas DC, Calvache LG, Caicedo JP, Calvache JA. Barreras y limitaciones en la implementación de la lista de verificación de la seguridad quirúrgica de la Organización Mundial de la Salud. Revista de la Facultad de Ciencias de la Salud Universidad del Cauca. 2014;16(1):32-43

Calvache JA, Chaparro LE, Chaves A, Delgado MB, Fonseca N, Montes FR, Moyano JR, Rubio J. Strategies and obstacles to research development in anesthesiology programs:consensus document in Colombia. Rev Colomb Anestesiol. 2012;40:256-61. DOI: https://doi.org/10.1016/j.rca.2012.07.001

II. Systematic, Non-systematic, invited and uninvited reviews, Editorials or short articles:

Delgado-Noguera MF, Forero Delgadillo JM, Franco AA, Vazquez JC, Calvache JA. Corticosteroids for septic arthritis in children. Cochrane Database of Systematic Reviews 2018, Issue 11. Art. No.: CD012125. DOI: 10.1002/14651858.CD012125.pub2.

Gómez JC, Calvache JA. The reflection paper. Rev Colomb Anestesiol. 2018;46(Sup):1-2. DOI:10.1097/CJ9.0000000000000037

Calvache JA. Editorial: Mejorando el reporte de la investigación a través de las indicaciones a los autores. Rev. Fac. Cienc. Salud Univ. Cauca. 2017;19(1):16-19.

Delgado-Noguera MF, Forero Delgadillo JM, Franco AA, Concha J, Vazquez JC, Calvache JA. Corticosteroids for septic arthritis in children (Protocol). Cochrane Database of Systematic Reviews 2016, Issue 3. Art. No.: CD012125. DOI: 10.1002/14651858.CD012125.

Castro-Delgado OE, Salas-Delgado I, Acosta-Argoty FA, Delgado-Noguera M, Calvache JA. Very low and extremely low birth weight. Pediatria. 2016;49(1):23-30. DOI:10.1016/j.rcpe.2016.02.002

Delgado-Noguera MF, Calvache JA, Bonfill Cosp X, Kotanidou EP, Galli-Tsinopoulou A. Supplementation with long chain polyunsaturated fatty acids (LCPUFA) to breastfeeding mothers for improving child growth and development. Cochrane Database Syst Rev. 2015 Jul 14;(7):CD007901. DOI: 10.1002/14651858.CD007901.pub3

Calvache JA, León E, Gómez LM, García C, Torres M, Buitrago G, Gaitán H. Evidence-based recommendations of postoperative complications management in the Colombian context. Rev Colomb Anestesiol. 2015;43(1):51-60. DOI: 10.1016/j.rca.2014.10.005

Calvache JA. About simulation and airway safety. Rev Colomb Anestesiol. 2014;42(4):309-11. DOI: 10.1016/j.rcae.2014.08.001

Miranda JD, Vallejos L, Ñañez D, Calvache JA. Errores en la administración de medicamentos intravenosos en pacientes sometidos a anestesia en el quirófano. Revista de la Facultad de Ciencias de la Salud Universidad del Cauca. 2013;15(1):23-28

Calvache JA, Klimek M. Riesgo absoluto, reducción absoluta de riesgo y riesgo relativo. Revista de la Facultad de Ciencias de la Salud Universidad del Cauca. 2012;14(4):20-21.

Ríos AM, Calvache JA, Gómez JC, Gómez LM, Aguirre OD, Delgado-Noguera MF, Uribe F, Lesaffre E, Klimek M, Stolker RJ. Sore throat complaints after elective surgery: cumulative incidence and risk factors. British Journal of Anaesthesia. 2012;108(suppl 2):ii310-ii367. DOI: 10.1093/bja/aer487

Arroyo L, Calvache JA. Ausencia de evidencia no es evidencia de ausencia. Revista de la Facultad de Ciencias de la Salud Universidad del Cauca. 2011;13(1):19-20.

Delgado-Noguera MF,Calvache JA, Bonfill Cosp X. Supplementation with long chain polyunsaturated fatty acids (LCPUFA) to breastfeeding mothers for improving child growth and development. Cochrane Database Syst Rev. 2010 Dec 8;(12):CD007901. DOI: 10.1002/14651858.CD007901.pub2

Chaparro-Gómez LE, Calvache-España JA, Arbeláez-León LM. Coadyuvantes analgésicos en dolor por cáncer. Utilización de la herramienta de preguntas clínicas de PubMed. Cirugía y Cirujanos. 2010;78:189-194.

Delgado-Noguera MF, Calvache-España JA, Bonfill-Cosp X. Supplementation with long chain polyunsaturated fatty acids (LCPUFA) in postpartum lactating women for improving development in breastfed infants (Protocol). Cochrane Database of Systematic Reviews 2009, Issue 3. Art. No.: CD007901. DOI: 10.1002/14651858.CD007901

III. Book chapters / E-learning / Applications:

Ramirez DE, Calvache JA. Design and performance evaluation of the "iTIVA" algorithm for manual infusion of intravenous anesthetics based on effect-site target". Rev Colomb Anestesiol. 2016;44(2):105-113. DOI: https://doi.org/10.1016/j.rca.2016.02.002

Calvache JA, Giraldo A. Reanimación con control del daño. In: Libro Nacional de Trauma. Sociedad Colombiana de Anestesiología y Reanimación, 4a Ed. 2017

Calvache JA, Delgado M. Epidemiologia Clínica y Medicina Basada en la Evidencia. Una aproximación. In: Tratado de Medicina Interna, Universidad del Cauca. 1a Ed. 2009

Calvache JA, Shoemaker R. Bioestadística e investigación en salud. In: Tratado de Medicina Interna, Universidad del Cauca. 1a Ed. 2009

TEACHING ACTIVITIES

2012 - present	Principles of Epidemiology in Health Care Universidad del Cauca, Colombia
2012 – present	Introduction to Data Analysis, Universidad del Cauca, Colombia
2012 – present	Critical Reading of Medical Literature Universidad del Cauca, Colombia
2014 - present	Systematic Reviews and Metanalysis Universidad del Cauca, Colombia
2014 – present	Introduction to Medical Research: Essential Skills Universidad del Cauca, Colombia
2015 – 2017	Introduction to Pain Management and Palliative Care Universidad del Cauca, Colombia
2013 – present	Supervising Research projects Department of Anesthesiology Universidad del Cauca, Colombia

DOCTORAL TRAINING

COURSES	Code	ECT
Erasmus Summer Program (10.2 ECT)		
Principles of Research in Medicine	ESP01	0.7
Clinical Decision Analysis	ESP04	0.7
Regression Analysis	ESP09	1.4
Methods of Public Health Research	ESP11	0.7
Clinical Trials	ESP14	0.7
Topics in Meta-analysis	ESP15	0.7
Pharmaco-Epidemiology	ESP21	0.7
Survival Analysis	ESP28	1.4
Introduction to Global Public Health	ESP41	0.7
Markers and Prognostic Research	ESP62	0.7
Advances in Epidemiologic Analysis	ESP64	0.4
Case-control Studies	ESP40	0.7
Cohort Studies	ESP39	0.7
Core Curriculum (21.4 ECT)		
Study Design	CC01	4.3
Classical Methods for Data-analysis	CC02	5.7
Clinical Epidemiology	CE02	5.7
Methodologic Topics in Epidemiologic Research	EP02	1.4
Modern Statistical Methods	EP03	4.3
Advanced Short Courses (6.5 ECT)		
Repeated Measurements in Clinical Studies	CE08	1.4
Courses for the Quantitative Researcher	EP17	1.4
Advanced Topics in Decision-making in Medicine	EWP02	1.9
Diagnostic Research	EWP05	0.9
Prognosis Research	EWP16	0.9
Skills Courses (2.65 ECT)		
Introduction to Medical Writing	SC02	1.1
Working with SPSS for Windows	SC04	0.15
Summer Course English	SC08	1.4
Research (33.1 ECT)		
Development Research Proposal	DRP	2.5
Oral Research Presentation	PRES	1.4
Research Period	EX	29.2
Research Period Stay (doctoral thesis)	n/a	20
Lectures & Conferences (selection) (5 ECT)		
15th WFSA World Congress of Anesthesiologists, Buenos Aires, Argentina (2012). (oral)	n/a	1.0
XVI Reunión Red Cochrane Iberoamericana, Medellín Colombia (2016). (3 oral)	n/a	1.0

Congreso Colombiano de Anestesiología, Cali, Colombia (2015). (oral)	n/a	1.0
The Ecosystem of Evidence. Evidence based healthcare teachers and developers GIMBE Foundation, Taormina, Italy (2017). (oral)	n/a	1.0
V Gran Sesión de Epidemiología, Cali, Colombia (2018). (oral)	n/a	1.0
- PhD Training = 63.65 ECT		
- Presentations & Conferences = 5 ECT		
- Research Period Stay (doctoral thesis) = 20 ECT		
TOTAL = 88.65 ECT		