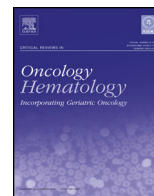




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Sympathetic blocks for visceral cancer pain management: A systematic review and EAPC recommendations

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ABSTRACT

The neurolytic blocks of sympathetic pathways, including celiac plexus block (CPB) and superior hypogastric plexus block (SHPB), have been used for years. The aim of this review was to assess the evidence to support the performance of sympathetic blocks in cancer patients with abdominal visceral pain. Only comparison studies were included. All data from the eligible trials were analyzed using the GRADE system. Twenty-seven controlled studies were considered. CPB, regardless of the technique used, improved analgesia and/or decrease opioid consumption, and decreased opioid-induced adverse effects in comparison with a conventional analgesic treatment. In one study patients treated with superior hypogastric plexus block (SHPB) had a decrease in pain intensity and a less morphine consumption, while no statistical differences in adverse effects were found. The quality of these studies was generally poor due to several limitations, including sample size calculation, allocation concealment, no intention to treat analysis. However, at least two CPB studies were of good quality. Data regarding the comparison of techniques or other issues were sparse and of poor quality, and evidence could not be analysed. On the basis of existing evidence, CPB has a strong recommendation in patients with pancreatic cancer pain. There is a weak recommendation for SHPB, that should be based on individual conditions. Data regarding the choice of the technique are sparse and unfit to provide any recommendation.

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1. Introduction

Abdominal pain is common in patients with cancer. In a survey on prevalence, causes, and mechanisms of pain in advanced cancer patients followed at home, abdominal pain was present in 45% of the patients. Two-third of these patients had visceral pain, with mixed pain syndromes in more than half of the patients (Mercadante, 2007). Similarly, in a large international survey about 35% of patients presented visceral pain, usually with a visceral component mixed with somatic or neuropathic mechanisms (Caraceni and Portenoy, 1999). More recently breakthrough abdominal pain has been characterized (Mercadante et al., 2014). Undertreatment was often the principal cause of abdominal breakthrough pain and optimization of the analgesic therapy significantly reduced the number of patients with abdominal breakthrough pain episodes.

This observation underlines the need to achieve a good pain control of visceral pain syndromes. To date, different approaches have been suggested for treatment of abdominal and pelvic pain, including pharmacological, radiation, neuroinvasive, and neurolytic treatments. The neurolytic blocks of sympathetic pathways at different levels, including celiac plexus block (CPB) and superior hypogastric plexus block (SHPB), have been used for years. CPB has been used for the treatment of cancer pain originating from upper abdominal viscera, while SHPB is targeted for pelvic visceral pain. Different techniques have been developed in an attempt to achieve high success rate of analgesia and few procedural related complications (Mercadante and Nicosia, 1998). However, the definitive role of these techniques has to be defined. Therefore, we performed a systematic review of the existing data of sympathetic blocks for abdominal cancer pain management. This work was done within the European Palliative Care Research Network (EPCRN) as part of the project to update the European Association for Palliative Care (EAPC) recommendations for treatment of cancer pain. The aim of this initiative for the EAPC is through rigorous and sound methodology to review of the evidence of pain strategies in order to provide new guidelines for the treatment of cancer pain (Caraceni et al., 2012). The present systematic review was based on the following research question: “in adult cancer patients with abdominal pain, what evidence supports the performance of sympathetic blocks?”.

2. Methods

A systematic literature search on MedLine, Embase and Cochrane Central Register of Controlled Trials electronic databases was carried out from each database set-up date to 3rd February 2014; text words and MeSH/EMTREE terms have been used as described in Table 1, that reports the search strategy employed for MedLine; appropriately revised equivalent strategies were developed for Embase and Cochrane Central Register of Controlled Trials. Hand search of the references list of identified papers was also performed.

A final list of the relevant abstracts was generated and divided between two of the co-authors (SM and AG) for reading. Each abstract was checked at least twice by two of the co-authors and selected according to the inclusion and exclusion criteria. Abstracts that matched the inclusion criteria and those with no clear information to be considered for exclusion were selected for full reading. Inclusion and exclusion criteria were reapplied and all articles that fitted with this review were analysed. The co-authors (SM and AG) discussed and resolved eventual doubts and disagreements regarding the studies of interest.

Studies were included if the interventional techniques were compared with analgesic drugs, or placebo, if they were conducted

in adult patients with cancer pain, if they contained relevant outcomes, and were written in English language. All data from the eligible trials were analyzed using the GRADE system, to define the quality of the evidence and to determine the strength of the recommendations for clinical practice.

Studies were excluded in case of double publications, if related to other clinical indications, or if they were reporting only complications from sympathetic blocks. Interventions were grouped according to the type of sympathetic block and choice of comparison.

The body of evidence derived from the studies was graded according to quality scoring system that ranges from +4 or A to +1 or D, where +4 or A=high quality (further evidence is unlikely to change confidence in the estimate of effect), +3 or B=moderate (further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate), +2 or C=low (further research is very likely to have an important impact on confidence in the estimate of effect and may change the estimate), and +1 or D=very low (any estimate of effect is very uncertain (Atkins et al., 2004). Evidence derived from randomized controlled studies received an initial score of +4. Points were subtracted or added depending on the following elements (Atkins et al., 2004; Working Group, 2014):

- Quality: based on study description of methodological concerns and limitations observed; grade decreased -1 point for serious limitation or -2 for very serious limitation (e.g., missing information or flaws regarding settings, sample size calculation, randomization/random list generation/allocation concealment, blinding, follow up and withdrawals, no intention to treat analysis, etc.).
- Consistency: degree of consistency of effect between or within studies; grade decreased -1 point in case of lack of agreement between studies (e.g., widely differing estimates of effects across studies, statistical heterogeneity, conflicting results, different results for different endpoints, etc.).
- Directness: the generalizability of population and outcomes from each study to population of interest; grade decreased -1 point for some uncertainty or -2 in case of major uncertainty about directness (e.g. inclusion of people outside group of interest, use of co-intervention, no direct comparisons between groups, small number of comparisons reported, unclear measurement of outcomes, short follow up, etc.).
- Imprecise or sparse data: wide confidence intervals, large *p*-value, small samples; grade decreased -1 point.
- High probability of bias: systematic error in the patient selection, outcomes measurement, or data analysis, small number of trials influenced by pharmaceutical industry sponsoring; grade decreased -1 point.

The strength of recommendations was elaborated based on the examined quality of evidence and classified in “strong for using the intervention”, “weak for using the intervention”, “weak against using the intervention”, and “strong against using the intervention”. The quality was assessed only for studies comparing sympathetic blocks with some other analgesic treatment.

3. Results

The initial search yielded 132 records. Eleven papers were duplicates, leaving 121 papers available for evaluation. Seven additional records were retrieved by hand search or cross-references. One-hundred-twenty-eight papers did not fit inclusion criteria. Seven papers were reviews (Fig. 1).

Table 1

Comparison between analgesic treatments. A=analgesics, CPB=celiac plexus block; TA=transaortic; S=splanchnicectomy; TS=toroscopic splanchnicectomy; spl= splanchnicectomy; intraop= intraoperative; SHPB= superior hypogastric plexus block; EUS=ultrasound endoscopy; CT= computed tomography; LB= lumbar sympathetic ganglion chain block; EP= epidural; LA= local aneestsics; R-C= randomized-controlled; R-C- DB= randomized controlled double blind; AE= adverse effects; Post= posterior approach; NA= not available.

Authors	Comparative groups	Techniques	Design	N°	Duration	Pain	Adverse effects Complications
Mercadante, 1993	CPB + A A	Post	R-C	20	Till death	=Pain score -opioid cons	-AE
Lillemoe et al., 1993 Staats et al., 2001	CPB + A PL + A	Intraop spl	R-C DB	137	Till death	+Pain score +Survival +Mood -Pain interference	NA
Kawamata et al., 1996	CPB + A A	Post	R-C	21	Ten weeks	+Pain score -Opioid cons -QoL deterioration	- AE
Polati et al., 1998	CBP + A LA + A	Post	R-CDB	24	Till death	=Pain score -Opioid cons	-AE
Shulman et al., 2000	CPB + A EP butamben + A	Post EP	C	24		=Pain score =Opioid cons	=AE
Okuyama et al., 2002	CPB A	Intraop	C	21	Till death	-Opioid cons	-AE
Jain et al., 2005	CPB A	Post	C	100	1 month	+Pain score -Opioid cons =QoL	-AE
Wong et al., 2004	CBP + A LA + A	Post	R-C DB	101	24 weeks	+Pain score =Opioid cons =QoL	=AE
De Oliveira et al., 2004	CPB/SHPB/LB early = morphine ≤90 mg≤ CPB/SHPB/LB late = morphine ≥90 m A	CPB/SHPB/LB	R-C	44	8 weeks	=Survival At any morphine dose CPB/SHPB/LB +pain score -Opioid cons +QoL	-AE
Johnson et al., 2009	CPB + A A	CPB TS	R-C	65	2 months	=Pain score =Opioid cons	=AE
Stefaniak et al., 2005	CPB/TS A	CPB/TS	C	98	8 weeks	+Pain score +QoL	NA
Zhang et al., 2008	CPB + A A	CPB CT post	R -C	56	3 months	+Pain score (2 weeks) -Opioid cons =QoL	-AE
Wyse et al., 2001	CPB + A A	EU	R-C DB	96	3 months	+Pain score =Opioid cons =QoL	NA
Amr and Makharita, 2013	Early CPB + A late CPB + A	Post	R-C	60	One year	=Survival -Pain score +Opioid cons -QoL	+AE
Mishra et al., 2013	SHPB + A A	EU	R-C	50	3 months	+Pain score -Opioid cons	=AE

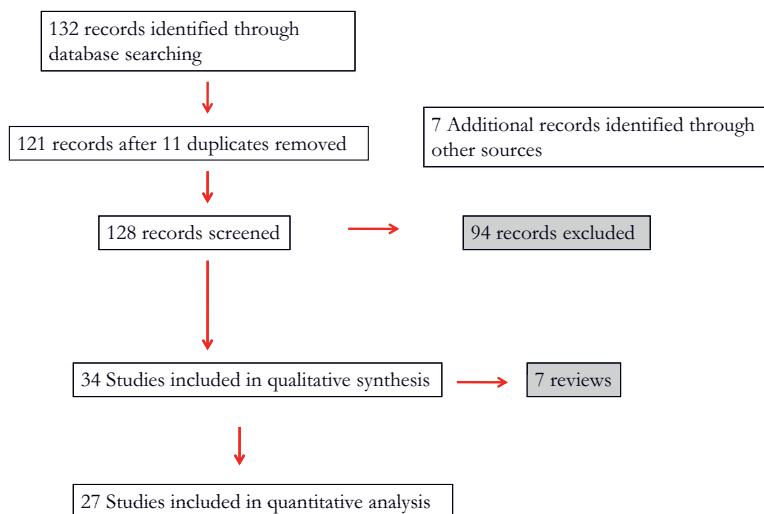


Fig. 1.

3.1. CPB

For CPB there are more consistent data regarding the different techniques, anatomical sites or injections, or comparison with traditional analgesic treatments.

a) CPB or splanchnicectomy versus analgesics or other treatments

In 14 papers CPB, performed with different approaches, was compared with analgesics or saline. In the first comparison study by Mercadante et al. (Mercadante, 1993), CPB and analgesics were compared with analgesics only in patients with pancreatic cancer, who had well-controlled pain analgesics given for a week before starting the study. A decrease in opioid consumption and less adverse effects were found in CPB+analgesic group, while no differences in pain score were reported. In a similar study by Kawamata et al. (Kawamata et al., 1996), 21 patients with pancreatic cancer were randomized to receive CPB or analgesics. CPB patients had a significant decrease in pain intensity and morphine consumption in comparison with patients using standard analgesics. Less deterioration of quality of life was also reported. Polati et al., (Polati et al., 1998) compared 12 patients treated with CPB with 12 patients treated with standard analgesics. They reported an immediate better pain relief and less adverse effects in patients who received CPB compared with those treated with analgesics, although long-term results did not differ. Intraoperative splanchnicectomy or saline injection was performed by Lillemoe et al. (Lillemoe et al., 1993) in a double-blind manner, regardless the presence of pain in 137 patients with pancreatic cancer. The block significantly reduced pain scores or delayed the onset of pain in patients without pre-existing pain. Moreover, a marked improvement of survival was unexpectedly reported. In a further analysis CPB improved pain, elevated mood, and reduced pain interference with activity (Staats et al., 2001). In another study by Okuyama et al. (Okuyama et al., 2002), including 21 patients, intraoperative CPB was compared to pharmacological therapy (15 and 6 patients, respectively). Patients were prevalently receiving anti-inflammatory drugs. Analgesic consumption did not decrease in the first observation period of one week, but differences between the groups were reported in the subsequent weeks. This study did not report pain scores. Surprisingly, survival was longer in CPB group.

In a randomized-controlled double blind study in a larger number of patients Wong et al. (Wong et al., 2004) observed that CPB improved pain relief, but did not affect quality of life or survival, in comparison with a group receiving a sham procedure with local anaesthetics. In a non-randomized study by Jain et al. (Jain et al., 2005), one group which also included patients with poor conditions unsuitable for an interventional procedure, received standard analgesic treatment, while patients receiving analgesics but who reported less than 50% of pain relief, underwent CPB. CPB patients had lower pain scores, morphine consumption, and adverse effects and better performance status, but no differences in quality of life.

Zhang et al. (Zhang et al., 2008) compared in a controlled study CPB guided by computerized tomography (CT) with a standard analgesic treatment. Pain scores were significantly lower in CPB group, but no differences were found after 14 days. Opioid consumption and adverse effects were lower in CPB group, but no differences in quality of life were found.

Two techniques, including traditional CPB or thoracoscopic splanchnicectomy (TS) were compared with the use of standard analgesics for abdominal cancer pain. Effective pain relief was achieved in about half of patients two months after the procedures, without significant differences between the groups in pain scores, opioid consumption, and adverse effects (Johnson et al., 2009). In another non-randomized study, both CPB and TS were beneficial

and resulted in a better quality of life in comparison with patients treated with standard analgesic therapy (Stefaniak et al., 2005).

In a study by Wise et al. (Wyse et al., 2001), 96 patients with positive biopsy for suspected pancreatic cancer performed by endoscopy, were randomly assigned to an early CPB or conventional treatment with analgesics. CPB provided a better pain relief at 1 month and at 3 months intervals. Morphine consumption was similar in both groups at 1 month, and no effects on quality of life or survival were observed.

Amr et al. (Amr and Makhirita, 2013) performed CPB early at first consultation or when pain was already controlled by analgesics. A significant decrease in pain intensity and a better quality of life was observed after 1–2 months in patients who had been previously treated by analgesics. Moreover, in this group morphine consumption and adverse effects were lower. Finally, Shulman et al. (Shulman et al., 2000) compared CPB with epidural butamben, a material-based delivery system of a local anesthetic that produces a long-lasting epidural analgesia, in patients with uncontrolled pancreatic pain. No differences in duration of pain relief and opioid consumption between the two groups were found.

De Oliveira et al. (De Oliveira et al., 2004) compared CPB, SHPB, or lumbar sympathetic ganglion chain block in patients receiving low (≤ 90 mg) and high doses (>90 mg) of oral morphine. One group received pharmacological therapy only. Blocks performed in both patients receiving low and high opioid doses resulted in a better decrease of pain, reduced opioid consumption, and provided a better quality of life, in comparison with analgesics only. Blocks were equally effective regardless of the level of previous opioid doses. The quality of the studies regarding CPB, according to the GRADE system, are reported in Table 2.

b) SHPB

Only one controlled study of SHPB was found. Mishra et al., (Mishra et al., 2013) randomized fifty patients with pelvic cancer pain associated with gynaecological cancer to receive either ultrasound-guided SHPB and oral morphine or oral morphine only. Patients treated with the block had a decrease in pain intensity and a less morphine consumption, while no statistical differences in adverse effects were found. The quality of this study according to the GRADE system, was very poor due to several limitations, including sample size calculation, allocation concealment, no intention to treat analysis.

c) Comparison among techniques

Three posterior techniques for CPB, including transaortic, classical, or splanchnicectomy, were compared in patients with pancreatic cancer pain. No differences were found between the techniques in terms of immediate and long-lasting complete pain relief. Pain relief was more pronounced when the blocks had been performed early, before opioid therapy or when patients were receiving anti-inflammatory drugs (Ischia et al., 1992). CPB performed with different imaging guidances and TS provided similar pain relief, opioid consumption, and adverse effects (Johnson et al., 2009). In another study, transaortic CPB was compared with posterior splanchnicectomy (S). Codeine consumption and pain intensity significantly decreased in group S in comparison with CPB patients who, however, had a significant longer survival (Ozyalcin et al., 2004). No differences were found between using one or two injections of alcohol and local anesthetics by endoscopic ultrasound (EUS)-guided CPB, and both safety and survival were similar (LeBlanc et al., 2011). In a comparison non-controlled study, CT and EUS guidance for CPB produced a similar technical success (Marcy et al., 2001), and in a randomized-controlled double blind study CT and EUS-guidance provided similar pain control and quality of

Table 2
CPB: studies graded by quality of evidence.

Authors	Limitation	Directness	Imprecise or sparse data	High probability of bias	Quality of evidence
Mercadante, 1933	-2		-1		Very low quality
Lillemoe et al., 1993	-1	-2		-1	Very low quality
Kawamata et al., 1996	-2		-1		Very low quality
Polati et al., 1998	-2		-1	-1	Very low quality
Shulman et al., 2000	-2	-1	-1	-1	Very low quality
Staats et al., 2001	-1	-1		-1	Very low quality
Okuyama et al., 2002	-2	-1	-2	-1	Very low quality
Jain et al., 2005	-2	-1	-1		Very low quality
Wong et al., 2004					High quality
De Oliveira et al., 2004	-2	-1	-1	-1	Very low quality
Johnson et al., 2009	-2	-1	-1	-1	Very low quality
Stefaniak et al., 2005	-2	-1	-1	-1	Very low quality
Zhang et al., 2008	-2	-2	-1	-1	Very low quality
Wyse et al., 2001					High quality
Amr and Makharita, 2013	-1			-1	Very low quality
Mishra et al., 2013	-2		-1	-1	Very low quality

life, but CT-guidance needed less trails and re-blocks (Radpay et al., 2009).

Ugur et al. (2007) compared CPB traditionally performed with 2 needles or a long guided needle technique (two stylets). Fluoroscopy injection time was significantly shorter with the long guided needle technique (Ugur et al., 2007). Finally, in a mixed population of patients with pancreatic cancer or pancreatitis, CPB with EUS guidance was traditionally performed in the first group of patients, and a bilateral CPL EUS-guided was performed in a subsequent group of patients. The bilateral technique provided better pain scores than with the traditional approach (Sahai et al., 2009).

Two techniques of SHPB have been compared. Transdiscal and traditional posterior approaches were compared in thirty patients with pelvic cancer patients. Both treatments were effective in reducing pain intensity, but transdiscal approach produced fewer complications (Gamal et al., 2006).

d) Other issues

The effects of an injection of different volumes of alcohol, 10 mls or 20 mls, for CPB EUS-guided was assessed by Le Blanc et al. (LeBlanc et al., 2011). Similar clinical outcomes and complication rate were reported. In another study the efficacy of CPB was examined according to varying locations of pancreatic cancer. The block proved to be more effective in patients having tumor involving the head of pancreas, rather than the body or pancreatic tail. Moreover, in case of advanced tumor proliferation the analgesic effect of CPB was not satisfactory (Rikowski and Hilgier, 2000).

Patients who had a diagnostic block with local anesthetics before CPB were compared with patients who were directly treated with CPB. Although a positive response to diagnostic block correlated positively with CPB, it was a poor predictor when the response was negative (Yuen et al., 2002).

4. Discussion

Existing literature has afforded different aspects of neurolytic sympathetic blocks for the management of visceral cancer pain. Comparison studies assessed several points, including comparison with analgesic treatments, or different techniques. In a previous attempt of meta-analysis a low statistical evidence for the superiority of pain relief over analgesic therapy, was reported (Arcidiacono et al., 2011). In the present review a group of experts of EAPC analyzed the use of sympathetic blocks from different perspectives and graded the efficacy of these interventions according to standardized methods to provide recommendations for

clinicians. Moreover, some practical aspects in cancer patients with abdominal pain have been discussed as a source for future research.

a) CPB or splanchnicectomy

There is some evidence that CPB, regardless of the technique used, may provide improved analgesia and/or decrease in opioid consumption, and as a consequence a decrease of opioid-induced adverse effects, in comparison with a conventional analgesic treatment. This observation has been reported in a sufficient number of patients in randomized controlled studies, prevalently in pancreatic cancer pain (Mercadante, 1993; Kawamata et al., 1996; Polati et al., 1998; Lillemoe et al., 1993; Staats et al., 2001; Okuyama et al., 2002; Wong et al., 2004; Jain et al., 2005; Zhang et al., 2008; Stefaniak et al., 2005; Wyse et al., 2001; De Oliveira et al., 2004). Only one paper did not show any difference (Johnson et al., 2009).

Some controversies still remain, particularly regarding the most appropriate timing for performing such a block. Some studies, for example, have suggested an early intervention (Polati et al., 1998; Lillemoe et al., 1993; Staats et al., 2001; Ischia et al., 1992). This observation remains unproven (Wyse et al., 2001). In these studies the block was often performed in patients receiving step I or very low doses of opioids, or even in patients with no pain. One study compared different sympathetic blocks to patients who were receiving low doses of opioids (<90 mg/day or oral morphine equivalents) or higher dose of opioids (>90 mg/day or oral morphine equivalents), with the use of standard analgesics only. No differences between low and high dose opioid groups were observed (De Oliveira et al., 2004). Of interest, the level of opioid consumption does not reflect automatically the stage of disease. This issue has been recently re-examined. The effect of first controlling severe pain with medications and then performing the CPB was compared with an early procedure followed by analgesic medications according to the severity of pain. Controlling pain with analgesics and then performing the CPB was more effective than an early block, performed at beginning and followed by pharmacotherapy (Amr and Makharita, 2013).

An observational study in potential candidates to CPB or SHPB, showed that analgesic treatment with low doses of opioids can maintain adequate pain relief in most patients with abdominal-pelvic pain (Mercadante et al., 2002). It is likely that the success rate depends on the anatomical distribution, which can be distorted when the disease is locally advanced. Importantly, if the disease involves other areas of pain innervation, for example somatic areas such as peritoneum or diaphragm, the block will lose its effect, as the procedure aims to block the sympathetic pathways for visceral pain only. Even though this procedure can be performed

earlier, when pain would be exclusively visceral in nature, patients would eventually require analgesics because of the subsequent neural and somatic structure involvement, which is unpredictable (Mercadante, 2003). It has been reported that the probability of patients remaining completely pain-free after CPB diminishes with increasing survival time (Ischia et al., 1992). An early block performed in absence of pain, could be less useful in some circumstances, as pain evolution is unpredictable and the patients could remain pain-free or require only low doses of opioids until death (Mercadante et al., 2002). On the other hand, a block performed in a very advanced stage of disease could be unsuccessful because somatic structures may be involved. The decision should be based on a clear information to patients to find a compromise regarding the capability to reduce opioid consumption or their adverse effects for an imprecise period of time, ranging about 1–3 months.

Complications are rare, and occasionally reported in literature as case reports. Sympathetic blocks are claimed to be safe, because neurological complications are unlikely, differently from neurolytic somatic blocks. However, no study assessed complications as primary outcome. Given that severe complications are rare, it is assumed that some hundreds of patients should be recruited to assess the real complication rate and severity.

Quality of life has also been examined in a minority of studies. Less deterioration or better quality of life with CPB has been reported in some studies (Kawamata et al., 1996; Stefaniak et al., 2005; De Oliveira et al., 2004). However, in a similar number of papers no particular improvement of quality of life with CPB has been found (Wong et al., 2004; Jain et al., 2005; Zhang et al., 2008). In advanced cancer patients it is quite unlikely that a procedure, which may decrease pain intensity or opioid consumption, is able to improve quality of life in a complex clinical situation.

Another controversial point, but potentially relevant, is the prolongation of survival after performing a CPB, reported in some papers (Lillemoe et al., 1993). Unexplainably, survival rate was lower in CPB patients in comparison with bilateral splanchnic block (Ozyalcin et al., 2004). Also other papers have reported similar observations, for example with implantable intrathecal pumps for analgesic therapy (Smith et al., 2002). These findings have never been explained. On the other hand, other studies did not confirm this observation. Thus, there is no proof that a better pain control obtained with CPB or a reduction of opioid consumption in comparison with traditional pharmacological approach, may prolong survival (Wong et al., 2004; Johnson et al., 2009; Stefaniak et al., 2005).

Globally, consistency among studies is relatively poor. In general, in comparison with analgesic treatments alone, CPB provides a better pain relief or a decrease in opioid consumption in most studies, and in some cases a reduction of adverse effects. Two studies performed with two different techniques (Wong et al., 2004; Wyse et al., 2001), have shown strong evidence supporting that CPB provides an improvement in pain relief and reduces opioid consumption, although quality of life and survival do not seem to be affected. On the basis of examination of quality of studies, there is a strong recommendation in favour of CPB.

b) SHPB

Only one controlled study has been performed. SHPB produced a significant decrease in pain intensity and a less morphine consumption in comparison with pharmacological approach, while no statistical differences in adverse effects were found (Mishra et al., 2013). Pelvic pain is even more complex than pancreatic pain, for which CPB is performed, and often multiple pain mechanisms are involved. Somatic pain and neuropathic pain often coexist and mixed syndromes are more likely to be observed in patients with pelvic tumors than in those with abdominal pain caused by

pancreatic cancer (Mercadante et al., 2002). Thus, interruption of sympathetic pathway is not a guarantee for abolishing all kinds of pain inputs. There is weak recommendation for using the intervention.

c) Techniques

Data regarding techniques are more controversial and insufficient to provide recommendations on the choice of technique, in terms of efficacy, adverse effects, and complications. It is likely that the most familiar technique remains the best, although TC or US-guided procedures should potentially facilitate a more correct position of the needles and a better evaluation of the spread of contrast medium.

5. Conclusion

There is high quality evidence of the analgesic efficacy of CPB in patients with pancreatic cancer pain. The level of evidence on the reduction of opioid consumption and of opioid side effects is not as good. The techniques used in the best two studies are different and were done in a special context by very experienced professionals (Wong et al., 2004; Wyse et al., 2001). For this reason we suggest a strong recommendation to perform the procedure based on an individual evaluation of each patient, balancing the possible advantages and disadvantages in a specific clinical situation. Complications are rare, especially with modern imaging-guides. Data regarding the choice of the technique are sparse and unfit to provide any recommendation.

Data regarding SHPB are limited, also considering that a pure visceral mechanism is less likely to be found in a pelvic pain syndrome in comparison with pancreatic cancer. Therefore, at moment, there is a weak recommendation for this procedure, that should be based on individual conditions.

Authors' declaration

Dr. Mercadante and dr. Giarratano had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs. Mercadante, Kurita, Klepstad, and Sjogren designed the study protocol. Dr. Mercadante managed the literature searches and summaries of previous related work and wrote the first draft of the manuscript. Dr. Kurita, Klepstad, Sjogren, and Giarratano provided revision for intellectual content and final approval of the manuscript. All authors have no conflicts of interest to report, or received any remuneration, reimbursement or honorarium in any other manner. The authors are not affiliated in any manner with industries. No Funding/Support to be disclosed.

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