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Narrative Review

Catheter-based Techniques for Terminal Cancer Pain: A Review of Nonneuraxial Interventions with Clinical Implications for End-of-Life Pain Management

Edward Podgorski III, MD[1], Larry Driver, MD[1], Amitabh Gulati, MD[2], and Salahadin Abdi, MD, PhD[1]

From: [1]Department of Anesthesia, Perioperative Medicine and Pain Management, University of Texas Anderson Cancer Center, Houston, Texas; [2]Department of Anesthesia and Critical Care, Memorial Sloan Kettering Cancer Center, New York, New York

Address Correspondence: Edward Podgorski III, MD 1515 Holcombe Blvd. Houston, TX, 77030 E-mail: empodgorski@mdanderson.org

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Background: Evidence suggests that a significant proportion of terminal cancer patients have uncontrolled or inadequately controlled pain when using the World Health Organization (WHO) analgesic ladder approach. The use of interventional techniques has proven to reduce pain that is refractory to conventional methods. However, despite the use of well-established techniques (e.g., intrathecal drug delivery, celiac plexus blocks, etc), nonneuraxial, catheter-based techniques remain underutilized.

Objective: The purpose of this narrative review is to examine the evidence for nonneuraxial, catheter-based techniques in treating terminal cancer pain, the barriers to implementation, and its role in bridging the gap between single shot techniques and surgically implanted devices.

Study Design: This is a narrative review article summarizing case reports, case series, retrospective studies, prospective studies, and review articles published at any time frame on the use of nonneuraxial, catheter-based techniques for the treatment of cancer pain in the end-of-life setting.

Setting: The University of Texas MD Anderson Cancer Center.

Methods: A literature search was conducted from November 2020 to January 2021 using the PubMed database and keywords related to nonneuraxial catheters, terminal cancer pain, and hospice. All English-based literature published at any time frame involving human patients was included.

Results: The number of studies referencing the use of nonneuraxial, catheter-based techniques for the treatment of terminal cancer pain is limited (n = 25). All of these studies were small, single-center, nonrandomized, noncontrolled case series and case reports. A total of 63 patients were evaluated across all studies, with the largest study involving 12 patients. The most common medication used was monotherapy with bupivacaine or ropivacaine and the longest duration of continuous catheter usage was 217 days. Of the studies that reported outcomes, the majority reported a reduction in pain. Very few studies reported catheter-related adverse events and tunneling appeared to be an important factor in reducing complications.

Limitations: No studies were available comparing the use of nonneuraxial, catheter-based techniques to conventional systemic medical management. Further, the studies in this review were heterogenous and limited to a small sample sizes reported in case reports and case series only.

Conclusion: Nonneuraxial, catheter-based techniques have the potential to play a significant role in the treatment of terminal cancer pain. Despite limited data, initial findings indicate that nonneuraxial, catheter-based techniques have the potential to bridge the gap between single shot interventions and surgical implanted devices by providing an effective, continuous therapy, with a lower risk profile.

Key words: Cancer, catheter, continuous, end-of-life, pain, terminal

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The number of patients entering hospice continues to increase as the population in the United States ages. From 2017 to 2018, the number of Medicare beneficiaries receiving hospice services increased by 4% from 1.49 million to 1.55 million. The most common diagnosis at the time of enrollment into hospice in 2018 was cancer, accounting for 29% of all principal diagnoses. Pain has frequently been reported as one of the most common symptoms experienced by these patients with a prevalence of 58-69% in patients with advanced or terminal disease (1-4). Despite adherence to the World Health Organization (WHO) analgesic ladder, 10-25% of patients have cancer pain that remains refractory to conservative measures and 25-77% have undertreated pain (1,5). Furthermore, the prevalence of uncontrolled pain increases as patients near the end of life, with some evidence suggesting a range of 34-54% (6,7). Finally, opioids, the mainstay of the WHO ladder, are associated with intolerable side effects (e.g., sedation, altered mental status, nausea, constipation, etc), suppression of cell-mediated and humoral immunity, lack of efficacy in certain pain states (e.g., neuropathic pain, bone pain), addiction, and diversion (8-11). These outcomes and risks suggest both a significant opportunity and need to overcome the limitations of conventional pain management for patients with terminal cancer.

In an attempt to treat cancer pain for patients refractory to conventional medical management, interventional pain techniques have been proposed as the fourth step of the WHO ladder (12). The principal interventional categories include neuraxial analgesia, minimally invasive vertebral procedures, sympathetic neurolysis, peripheral nerve blocks, neuromodulation, and neurosurgical procedures (1,13). While the evidence for many of these techniques in treating cancer pain is well established, the same cannot be said for peripheral nerve blocks, especially catheter-based techniques delivered to targets outside the neuraxis (11,13-16). A systematic review by Klepstad et al (14), published in 2015 found 16 papers, including a total of 59 cases, on the use of peripheral nerve blocks for cancer pain. An updated review in 2018 identified another 6 cases. Klepstad concluded that the use of peripheral nerve blocks for cancer pain is still anecdotal. Despite widespread acceptance of catheter-based techniques for the treatment and prevention of perioperative pain and recent advances in technology (e.g., ultrasound), these same techniques have not been widely applied to cancer pain management (17).

Currently, there is a void in the interventional management of terminal cancer pain. On one end of the spectrum, patients are offered less invasive interventions (e.g., splanchnic/celiac plexus) but often outlive medications delivered via these single bolus techniques. On the other end, patients have the option of more invasive, surgical techniques involving the neuraxis (e.g., intrathecal drug delivery devices, cordotomy); however, many patients are considered poor candidates for these procedures, or there are concerns about the risk-benefit balance. Catheter-based techniques outside the neuraxis can help bridge this gap by providing continuous, sustainable therapy, with a balanced risk profile, level of invasiveness, and degree of technical complexity compared to existing interventions.

Methods

A literature search was conducted from November 2020 to January 2021 using the PubMed database with no date restriction. The search focused on continuous catheters used outside the neuraxis (e.g., peripheral nerves and sympathetic targets) for the treatment of cancer pain in end-of-life or terminal patients. Search terms utilized for inclusion criteria were: "continuous peripheral nerve block;" "long term use of nerve block catheters;" "tunneled catheters;" "indwelling catheters;" "permanent catheters;" "infusions;" "cancer pain;" "palliative;" "end-of-life;" "terminal;" and "hospice." The following keywords were excluded: "perioperative;" "surgical;" "surgery;" "urology;" "urinary;" "ascites;" "effusions;" "noncancer;" "intrathecal;" "intravenous;" and "epidural." All English-based literature reporting clinical data involving human patients was included, with no restriction on the year of publication. Literature included all prospective and retrospective, randomized and nonrandomized data. A manual search of the citation lists from seminal review articles and the literature collected from the PubMed search was performed and appropriate literature was added.

Results

Study Details and Patient Demographics

A total of 25 case reports and case series on the use of nonneuraxial continuous catheter-based techniques to treat pain in terminal cancer patients have been reported in PubMed since 1993, with less than half (n = 11) of these studies being published in the last decade and none involving randomized controlled trials (Table 1). The number of patients included across all

Table 1. *Summary of Nonneuraxial Catheter-based Techniques in Terminal Cancer Patients*

Study	Type of Study	# Patients (Age range)	Cancer Diagnosis (n)	Type of Block, Technique, Tunneled (Y/N), Location, Abx (Y/N)	Medication & Rate +/- bolus	Duration (days)	Removed (Y/N) - reason	Died	Catheter Setting	Pre-Procedure NRS	Post-Procedure NRS	Side Effect(s)/ Adverse Reaction(s)
Anghelescu et al 2010 (16)	Case series	3 (13 - 18)	Osteosarcoma (2), Burkitt's (1)	Femoral (1), Lumbar plexus (1), Interscalene (1), NS, NS, NS, NS	0.2% ropi @ 8-12 mL/h (2) 0.2% bupi @ 12 mL/h	(3 - 81)	N (1), Y – NS (2)	Y	Hospital, Home (2)	NS	NS	NS
Aydin et al 2018 (58)	Case report	2 (40 - 68)	Lung (1), Mesothelioma (1)	Erector spinae, US/ fluoro with contrast, Y, NS, NS	0.25% bupi 10 mL tid	NS	NS	NS	NS	7.5 - 9	1.5 - 3	NS
Buchanan et al, 2009 (59)	Case report	1 (66)	Renal	Interscalene, US, Y, NS, NS	0.2% ropi 5 mL/h	10	Y - 1d dislodged, 10d pain controlled	NS	Home	6	1.5	Dislodged, sensory deficits
Burgoyne et al 2012 (35)	Case report	3 (8 - 14)	Osteosarcoma (3)	Femoral (2), Interscalene (1), NS, Y, OR, Y	0.2% ropi @ 6-8 mL/hr	33 - 41	Y (3) - pain controlled, obstruction, MRI	NS	Home (2)	NS	NS	Obstruction (1)
Choi et al 1999 (60)	Case report	1 (71)	Rectosigmoid	Inferior mesenteric ganglion, Fluoro, Y, OR, N	0.1% bupi @ 8 mL/h	4	Y - pain controlled	NS	Hospital	NS	3.5	NS
Cooper et al 1994 (61)	Case report	1 (64)	Osteosarcoma	Interscalene, stim, N, OR, N	0.25% bupi bolused (not specified)	5	Y - leak	NS	Hospital	NS	NS	Leak
Esch et al 2019 (23)	Case series	2 (53 - 74)	Pancoast (2)	Paravertebral, anatomic (1), stim (1), Y, NS, NS	0.2% ropi @ 2 - 4 mL/h	40-44	N (1), Y (1) - leakage/ infectious skin changes	Y	Home (1)	NS	NS	leakage/ infectious skin changes (1)
Fischer et al 1996 (62)	Case report	2 (46 - 80)	Breast	Subclavian, stim, NS, NS, NS	0.25% bupi @ 4 mL/h	5	Y - pain controlled	Y	Hospital (1)	NS	NS	NS
			Ovarian	Femoral, stim, NS, NS, NS	0.25% bupi + fentanyl 5ug/mL @ 4 mL/h	10	Y - pain controlled	Y	NS	NS	NS	NS
Fuzier et al 2016 (11)	Case series	5 (52 - 59)	Desmoid (1), Myelodysplasia (1), Breast (1), Renal (1), Sarcoma (1)	Radial (1), Median (1), Interscalene (1), Femoral (1), Sciatic (1), US, Y, OR, NS	0.2% ropi @1.5 - 5 mL/h + 2 - 7 mL/30min	12 - 110	Y (5) - pain controlled, bridge to surgery and radiation, leak	NS	Home (3)	7	0 - 2	Paresthesia (1), leak (1)
Fuzier et al 2018 (42)	Case report	1 (58)	Desmoid	interscalene, US, Y, NS, NS	0.2% ropi @ 2 mL/h + 3 mL q3h	45	Y - MRI, pain controlled	NS	Home	7.5	0	NS

Table 1. *Summary of Nonneuraxial Catheter-based Techniques in Terminal Cancer Patients*

Study	Type of Study	# Patients (Age range)	Cancer Diagnosis (n)	Type of Block, Technique, Tunneled (Y/N), Location, Abx (Y/N)	Medication & Rate +/- bolus	Duration (days)	Removed (Y/N) - reason	Died	Catheter Setting	Pre-Procedure NRS	Post-Procedure NRS	Side Effect(s)/ Adverse Reaction(s)
Gemayel et al 2015 (31)	Case report	2 (47 - 72)	Melanoma (2)	Interscalene (2), stim, NS, NS	0.125% bupi @ 4 mL/h	18 - 31	N (1), Y (1) – radiation therapy	Y	Home	8 - 10	0	NS
Hakim et al 2015 (43)	Case report	1 (24)	Osteosarcoma	Subclavian/ Interscalene, US, NS, OR, NS	0.2% ropi @ 6 mL/h	8	Y - pain controlled	NS	Home	7	NS	NS
Kaki et al 1998 (20)	Case report	1 (47)	Lung	Lumbar plexus, fluoro, NS, OR, NS	0.25% bupi 0.25% @ 5 mL/h + neurolysis	3	Y - neurolysis	NS	Hospital	9	0.5	sensory and motor weakness
Kalagara et al 2019 (15)	Case report	1 (55)	Pancoast	Erector spinae, US, NS, NS, NS	0.2% ropi @ 5 mL/h	9	Y - leukocytosis (no infection identified)	NS	NS	9	4	leukocytosis (no infection treated)
Khor et al 1996(9)	Case report	1 (39)	Renal	Femoral, anatomic, Y, OR, Y	0.25% bupi bolused (NS)	47	Y - replaced with portacath	Y	Hospital, Home	NS	2	NS
Kohase et al 2004 (21)	Case report	1 (74)	Orofacial	Trigeminal, NS, NS, NS	0.25% bupi @ 0.5 mL/h + neurolysis	7	Y - neurolysis	Y	NS	NS	NS	NS
Mercadante et al 1995 (45)	Case report	1 (68)	Lung	Suprascapular, anatomical/ fluoro with contrast, Y, NS, NS	0.5% bupi 5 mL tid	NS	N	NS	Home	NS	NS	NS

Abbreviations: NS – not specified; stim – stimulation; fluoro – fluoroscopy; Y – yes; N – no; S1- sacral nerve root 1; bupi – bupivacaine; ropi – ropivacaine; cath – catheter; tid – three times daily

studies totaled 63, with the largest case series involving 12 patients. Patient ages ranged from 8 to 83 years. Most (n = 23) of the studies were in the adult population with 2 studies being conducted in the pediatric population. The 3 most common cancers reported were lung (12/63, 19%), sarcoma (9/63, 14%), and breast (5/63, 8%). A majority of patients were reported to have pain refractory to a combination of high dose opioids and adjuvant medications.

Procedures

Target locations ranged from individual peripheral nerves (e.g., radial, median) to more diffuse structures (e.g., sympathetic plexus), with celiac (12/63, 19%), intrapleural (10/63, 16%), and interscalene (9/63, 14%) catheter locations being the most common. A variety of techniques for catheter placement were used equally, including ultrasound guidance, fluoroscopy, stimulation, and placement using anatomical landmarks. Subcutaneous catheter tunneling was performed in the majority of patients (39/63, 62%) undergoing this technique. Although some studies specified the location of performing the procedure as either in the operating suite or in the procedure room, reporting was not consistent across all studies. This was also true of pre-operative antibiotic use, with most studies not commenting on antibiotic usage. Of the 5 studies that did report using pre-operative antibiotics, dosage strategies and choice of antibiotics varied.

Medications and Catheters

Bupivacaine was the dominant choice (46/63, 75%) of local anesthetic, with all other catheters employing ropivacaine. Rates and concentrations of continuously administered bupivacaine ranged from 0.5 mL/h to 15 mL/h and 0.1% to 0.375%, respectively. Ropivacaine rates and concentrations ranged from 1.5 mL/h to 12 mL/h and 0.2% to 0.2%, respectively. Most of the infusion therapies used continuous delivery of one local anesthetic only. A few of the techniques employed combination therapy, including the study by Fischer et al (62), that used a combination of bupivacaine and fentanyl 5 mcg /mL at a rate of 4 mL/h and another study by Pacenta et al (18), using ropivacaine and clonidine 4 mcg/mL at a rate of 10 mL/h. Several studies utilized recurring boluses instead of continuous infusions, with studies by Vranken et al (19), Kaki et al (20), and Kohase et al (21), employing neurolysis in addition to delivery of local anesthetics. Few studies identified the delivery method for these medications, but types of delivery included elastomeric devices and electrically driven pumps. While some catheters were replaced more than once for a single individual, the longest duration of catheter therapy recorded was 217 days, documented as 31 weeks in the study by Vranken, et al (22). Mean and median catheter duration across all studies was 47 and 38 days, respectively, with a range of 3 to 217 days. Of the studies that reported catheter removal, adequate pain control was the most common reason (9/24, 37.5%), followed by MRI (4/24, 16.7%), and leakage (3/24, 12.5 %). Only 2 catheters were removed because of concerns of infection, with a case by Esch et al (23), reporting infectious skin changes and another case by Kalagara et al (15), reporting leukocytosis with no identifiable infection. Other reported reasons for removal include dislodgement and obstruction.

Outcomes

Eighteen of the studies reported both pre- and post-catheter NRS pain scores on a scale of 1-10 (with 10 being the most intense pain). The average pre-catheter and post-catheter pain scores in these studies were 7.9 and 1.5, respectively. A single patient in the study by Myers et al (24), reported an increase in their pain score after catheter placement from a 5/10 to 7/10. These studies were heterogenous in patient diagnosis, catheter technique, and timing of NRS scores. Furthermore, most of these patients received other therapies (e.g., systemic opioids) in addition to catheter infusions. Side effects and adverse reactions were reported infrequently, with most reports noting the reversibility of these events, including paresthesia, weakness, hypotension, etc. A total of 10 patients were reported to have died at home with the catheter in situ. Other reported catheter setting(s) at time of death include the hospital.

Discussion

Interventional techniques as a whole remain underutilized in the treatment of cancer pain (4,6). Increased utilization earlier in the disease course for patients at high risk for uncontrolled pain, patients with complex and mixed pain syndromes, and patients with aggressive cancers could help reduce the burden of pain at this critical time. One of the most understudied and underutilized interventional techniques for the management of terminal cancer pain is continuous, catheter-based techniques outside the neuraxis. Barriers to use are multifactorial, but key factors include lack of data, unfamiliarity with catheter-based techniques for terminal cancer pain, complications, and lack of infrastructure to support long-term catheter use. The following discussion will analyze these barriers in the context of the currently available evidence and offer potential solutions to increase safe and effective use of nonneuraxial catheter-based techniques for the management of terminal cancer pain.

The majority of data on catheter-based techniques has focused on the perioperative period. To date, there are no controlled trials of catheter-based techniques in the management of cancer pain at the end-of-life. This finding is consistent with our review which found only case reports and case series for the treatment of terminal cancer pain. Lack of evidence is likely multifactorial and includes such factors as candidate patients being identified too late in their disease process, the ethics of randomizing terminal cancer patients, and access to academic hospital settings that specialize in cancer pain management. To improve patient participation in future studies, it is prudent for physicians to include nonneuraxial, catheter-based techniques in their discussion with patients, educate their supportive care and oncology colleagues on the benefits of these techniques, and encourage early referrals (1,4). Furthermore, the quality of published studies is low, due to their small sample size, retrospective analysis, and inconsistences in the outcomes that were measured. Future research should focus on publishing large case series, prospective studies, and studies comparing conventional medical management (CMM) alone to CMM with nonneuraxial, catheter-based techniques and/or combination neuraxial and nonneuraxial catheter-based techniques. Outcome measurements should go beyond pain scores and include an analysis of patient preference, adverse events, risk mitigation strategies, reasons for failure/discontinuation, the infrastructure employed for long term use in both the hospital and home settings, delivery methods (e.g. elastomeric or electronic infusion pumps), cost effectiveness comparison of CMM to nonneuraxial and implantable catheters, and opioid analgesics (13). Given the long-term use of these catheters and likely deployment in the home or group setting, it would be prudent for future studies to focus on the management of catheters in the out-of-hospital setting.

The lack of validity, risk of complications, and unfamiliarity that causes hesitation in using nonneuraxial, catheter-based techniques in terminally ill patients is similar to what was previously experienced in the perioperative setting. Formally dismissed as too difficult and too risky, these techniques are now the standard of care as evidence has accumulated in contrast to previous arguments (e.g., lack of validity and risk of complications) (25,26). Despite differences in patient pathology (e.g. surgical pain versus tumor pain) and circumstances (e.g., opioid naïve vs opioid tolerant) many similarities exists. Evidence in the perioperative setting can guide practitioners on the application of these techniques in end-of-life patients until further evidence accumulates. Common oncologic and perioperative targets include the brachial plexus, femoral and sciatic nerves, paravertebral space, and erector spinae plane. Ultrasound and fluoroscopic techniques are well-established for these targets and thus standard practice can be followed for these procedures. Targets unique to terminal cancer patients include sympathetic and intrapleural targets. For these less commonly performed procedures, it is advisable that previous studies be thoroughly reviewed (e.g., Vranken's study (19) of celiac plexus catheters), and/or experts in cancer pain management be consulted. Procedures should also be performed in a tertiary care setting until the practitioner is comfortable with the procedure and managing any potential complications. Patients can also be referred to academic centers that specialize in cancer pain management. An important consideration in the cancer patient population is tumor involvement of the interventional target. Although this can complicate the placement of a catheter and distort the image seen on ultrasound, reports suggest that this factor did not necessarily interfere with proper placement (22). Other anatomical concerns include progression of disease to involve nerves not originally covered by the catheter and displacement of the catheter by tumor growth (8). One solution to these problems is to preemptively place the catheter more proximal; however, broader dermatomal coverage must be balanced with the potential of increased side effects. Another solution is to utilize fluoroscopy to help identify anatomy that is difficult to visualize on ultrasound. For certain procedures (e.g., deep plexus blocks) fluoroscopy, and CT guidance are preferable.

Medication usage also demonstrates similarities between settings. Comparable to the perioperative setting were the infusate of choice (bupivacaine or ropivacaine) and concentration. Infusion rates are also similar, but it is unclear if cancer patients require more total mg per day. We hypothesize that dose escalation is more likely in terminal cancer patients, especially in the last few days of life. Future research should report the total daily dose in mg per day, the pathology being treated, the target neural structure, and the quality of the pain (e.g., nociceptive or neuropathic) to better understand baseline requirements for future infusions. Until further evidence is generated it would be prudent for practitioners to start with the most commonly cited concentrations of local anesthetic (0.1 to 0.125% for bupivacaine and 0.1 to 0.2% for ropivacaine) and the lowest effective rate of infusion. Dose ranges currently available for terminal cancer patients (2 mL/h to 15 mL/h) can be used as an additional guide. Ultimately, these systems are titratable and should be adjusted to balance pain control and side effects. Furthermore, despite documented adjuvant (clonidine and fentanyl) use in both settings (Table 1), local anesthetics are the only FDA-approved medications for continuous perineural administration (27). Given the paucity of safety data and evidence, adjuvant medications are not recommended in standard practice (28-30).

For the majority of catheter-based techniques, medication regimens (e.g., basal alone, basal and bolus, or bolus alone) and delivery methods (e.g., single injections, elastomeric pumps or electronic pumps) are also similar; however, important differences exist, including duration of therapy, the logistics of managing catheters, and delivery devices outside of the hospital. Two major barriers to long term catheter infusions are catheter migration and infection. Data in the perioperative and cancer settings suggest several tactics for minimizing these complications, of which subcutaneous tunneling appears to be the most significant. Subcutaneous tunneling was commonly reported in studies in which catheters were placed for terminal cancer patients (62%), but was not often reported for perioperative catheters. This is likely the result of catheters being used for longer durations in the cancer population. The FDA has approved the use of catheters for infusions lasting no longer than 3 days, making longer use in the perioperative setting uncommon (31). Despite no prospective studies on tunneling, evidence suggests that tunneling may decrease the incidence of dislodgement and infection (27,31-33). For example, tunneled epidural catheters have demonstrated successful long-term use up to 240 days (34). Similar long-term durability was found for catheters used at the end-of-life, with one patient receiving therapy via a tunneled catheter for 217 days (22). Infection is postulated to occur from bacteria introduced at the catheter insertion site. Thus by increasing the distance between the nerve and catheter exit site, one can decrease the risk of infection (35). Improved outcomes have been demonstrated when tunneling was utilized in peripheral nerve block catheter procedures and high-risk ICU patients using central lines (18,36). Furthermore, studies have demonstrated a catheter colonization rate of 17-57% when no tunneling was used and 6.2% when tunneling was used (37). Despite evidence suggesting a correlation between catheter duration and risk of infection, no such correlation has been demonstrated when tunneling is utilized (37). Techniques other than tunneling that have been reported to help reduce migration include suturing (38), the use of adhesives (25,39), anchoring devices (25), and avoidance of highly mobile areas (22). Methods suggested to reduce infection include, the use of a subcutaneous port; avoiding moist areas (22); the use of coiled catheters (26); prophylactic antibiotics, for which optimal timing, dose, class of antibiotic and duration are unknown (31,40,41); the use of sterile infusates that are changed frequently (18,42); chlorhexidine-impregnated dressings (43); strict aseptic technique during catheter placement; filters (9,44); and the use of sterile dressings with frequent dressing type changes, for which the optimal dressing and replacement duration is unknown (44). Further investigation on which strategies are most effective is critical to decreasing complication rates and enabling long-term therapy.

Unique to the end-of-life setting is the infrastructure required for the successful use of catheter modalities at home. Although challenging, catheter-based techniques have proven to be effective and feasible in hospice patients using epidural and intrathecal devices at home (1). Similarly, studies on the successful use of catheter-based techniques outside the neuraxis for at-home pain management have also been reported (16,19,31,45). However, most of the evidence for non-neuraxial catheters comes from the peri-operative setting and data is still lacking on important topics, such as optimal medication delivery methods, caretaker responsibilities and qualifications, frequency and method of surveillance, and catheter and infusion management (46-53). Medication infusion systems have evolved to provide more ease of use, durability, flexibility, and cost-conscious options. These advancements are important to the success of long-term infusions in terminal cancer patients. In its simplest form, local anesthetic medication can be delivered manually as scheduled boluses; however, the benefits of basal infusions and logistical capabilities make automated systems preferable (54,55). The 2 most common delivery methods are elastomeric and electronic devices. Both methods are viable options for terminal cancer patients, especially as technology for elastomeric pumps has closed the gap with electronic devices. Importantly, both types of pumps have the capability to adjust basal rates, bolus volumes, and lockout times (56). Some of the key differences are listed in Table 2. No direct comparison can be made with studies in the perioperative setting because the use of specific devices was infrequently reported in studies involving end-of-life patients. One important advancement, which is particularly relevant for pain management at the end-of-life, is the ability to communicate remotely with electronic in-

Table 2. *Comparison of elastomeric and electronic infusion pumps.*

	Elastomeric (i.e., pressure driven)	**Electronic**
Accuracy	Over infuse 110-130%	Consistent +/- 5%
Easily portable (small size, weight, etc.)	Yes	No
Education required for use	Low	High
Audible alarms	No	Yes
Basal option	Yes	Yes
Bolus + lockout option	Yes	Yes
Reservoir location	Internal (not easily refilled)	External (easily refilled)
Cost (short term, perioperative infusion)	Less	More
Internet connectivity	No	yes

fusion pumps. These pumps provide clear advantages in the home setting and help to control breakthrough pain episodes and adverse events (e.g., insensate extremity) with a mean response time of 15 minutes (57). This new technology is encouraging and has the opportunity to provide the lowest cost, greatest flexibility, and highest patient satisfaction moving forward. Ultimately, delivery methods should be chosen on a case-by-case basis. For example, a patient that favors mobility would benefit from an elastomeric device that is portable. In contrast, a patient who is close to death would benefit from an electronic device that can be adjusted quickly and remotely for the fastest relief. Currently, data is lacking with regard to the optimal infrastructure required for long-term infusions and comparison data is needed to suggest the superiority of one method over another. Basic components to successful at home infusion system include education of caregivers (e.g., wound care basics and how to identify complications), a system for communicating with a supervising practitioner, supply chain infrastructure (e.g., local anesthetic bags, wound care supplies), and a monitoring program (e.g., remotely, in-person, or a combination) (19,31,43,57). Although this infrastructure can be challenging to create and manage, partnerships with nursing homes, hospice organizations, and infusion companies are available and encouraged.

Limitations

Data available for the treatment of end-of-life or terminal cancer pain using nonneuraxial, catheter-based techniques is limited to a small number of case reports and case series (n = 25). Furthermore, the number of patients included in these studies was also small, totaling 63 patients. Less than half of the studies were published within the last decade. No randomized controlled studies or comparison studies were found. These studies were heterogenous in their patient demographics, target, duration of catheter use, procedural technique, and outcomes measured. Of the patients who were discharged home with an indwelling catheter, few studies documented the detail of care of these catheters or methods used for long-term delivery of medications. Only one database, PubMed, was used for the literature search and no search was performed for abstracts presented at conferences. While these factors limit the ability to apply our findings broadly, the purpose of our review is to provide a foundation for further inquiry into the inclusion of catheter-based techniques in the treatment paradigm for pain in terminal cancer patients.

Conclusion

Treating cancer pain at the end-of-life is complex and requires a multimodal and multidisciplinary treatment strategy for success. This complexity has led to a significant proportion of cancer patients having uncontrolled pain at the end of life. Intimate knowledge of all modalities, including interventional techniques, is essential to helping control pain at this critical time. Based on the literature available and anecdotal experience, continuous nerve blocks outside the neuraxis are an underutilized and understudied interventional technique in the treatment of terminal cancer pain. These techniques have shown increasing acceptance and effectiveness in the perioperative period and may play an equally important role in reducing end-of-life pain. Specifically, they have the potential to fill the gap (Fig. 1) between single shot injections and more invasive surgical procedures, providing distinct advantages over other interventional techniques (Table 3). Further studies comparing nonneuraxial catheters to CMM or other interventional techniques and studies on optimizing effectiveness while reducing complications of these catheters will aid in increasing acceptance of nonneuraxial catheters and improve pain control at the end-of-life. A summary of key barriers to address and potential solutions for future study can be found in Table 4.

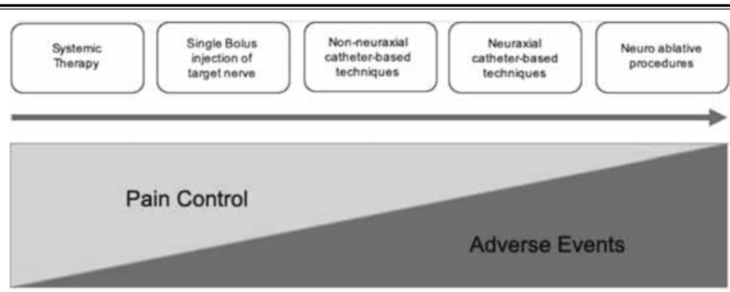

Fig. 1. *Interventional pain continuum.*

Table 3. *Advantages of nonneuraxial, catheter-based techniques in the treatment of terminal cancer pain.*

Indicated for local & diffuse pain (e.g., celiac, paravertebral, brachial plexus)	Long lasting (vs single-shot)	Decreases opioid usage
Titratable	Out of OR procedure (future application in home setting using ultrasound)	Can be used in home setting
Portable	Less risk of anticoagulation complications (vs. neuraxial infusions)	Easily reversible

Table 4. *Summary of key barriers and recommended solutions.*

Barriers	Solutions
Lack of data	Create national database to track hospice infusion systems; Publish large, prospective, comparison studies
Complications (migration and infection)	Tunnel catheters (migration); Daily inspection of catheter site and frequent dressing changes (infection)
Procedural technique and choice of drug infusion regimen	Refer to perioperative data
Choice of drug delivery device in hospice patients	Use electronic devices with internet capability for remote monitoring and faster titration
Infrastructure	Partner with hospice agency, nursing home, or infusion company; Utilize video conferencing

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