

# Does regional variation impact decision-making in the management and palliation of pancreatic head adenocarcinoma? Results from an international survey

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**Background:** Management and palliation of pancreatic head adenocarcinoma is challenging. End-of-life decision-making is a variable process involving multiple factors.

**Methods:** We conducted a qualitative, physician-based, 40-question international survey characterizing the impact of medical, religious, social, training and system factors on care.

**Results:** A total of 258 international clinicians completed the survey. Respondents were typically fellowship-trained (78%), with a mean of 16 years' experience in a university-affiliated (93%) hepato-pancreato-biliary group (96%) practice. Most (91%) believed resection is potentially curative. Most patients were discussed preoperatively by multidisciplinary teams (94%) and medical assessment clinics (68%), but rarely critical care (21%). Intraoperative surgical palliation included double bypass or no intervention for locally advanced nonresectable tumours (41% and 49% v. 14% and 85%, respectively, for patients with hepatic metastases). Postoperative admission to the intensive care unit was frequent (58%). Severe postoperative complications were often treated with aggressive cardiopulmonary resuscitation, intubation and critical care (96%), with no defined time points for futility (74%). Admitting surgeons guided most end-of-life decisions (97%). Formal medical futility laws were rarely available (26%). Insurance status did not alter treatment (97%) or palliation (95%) in non-universal care regions. Clinician experience, regional culture and training background impacted treatment (all  $p < 0.05$ ).

**Conclusion:** Despite remarkable overall agreement, geographic and training differences are evident in the treatment and palliation of pancreatic head adenocarcinoma.

**Contexte :** Le traitement et les soins palliatifs pour l'adénocarcinome de la tête du pancréas sont complexes. Les décisions de fin de vie reposent sur un processus hautement variable qui dépend de multiples facteurs.

**Méthodes :** Nous avons administré à des médecins un sondage international qualitatif à 40 questions afin de caractériser l'impact sur les soins exercé par différents facteurs, notamment médicaux, religieux, sociaux, relatifs à la formation et systémiques.

**Résultats :** En tout, 258 cliniciens ont participé à ce sondage international. Les participants étaient en général des spécialistes (78 %), cumulaient en moyenne 16 ans d'expérience dans le domaine hépatopancréatobiliaire (96 %) au sein d'un groupe affilié à une université (93 %). La plupart (91 %) ont dit croire que la résection est potentiellement curative. La majorité des cas faisaient l'objet de discussions préopératoires par des équipes multidisciplinaires (94 %) et en clinique d'évaluation médicale (68 %), mais rarement par une équipe de soins intensifs (21 %). Les soins palliatifs chirurgicaux peropératoires incluaient la double dérivation ou la non intervention en présence de tumeurs non résécables localement avancées (41 % et 49 % c. 14 % et 85 %, respectivement, chez les patients porteurs de métastases hépatiques). L'admission postopératoire aux soins intensifs a été fréquente (58 %). Les complications postopératoires graves étaient souvent traitées par réanimation cardiorespiratoire énergique, intubation et soins intensifs (96 %), sans critères chronologiques de futilité définis (74 %). C'est aux chirurgiens traitants que revenait la plupart des décisions de fin de vie (97 %). Peu avaient accès à des consignes formelles au sujet de la futilité des interventions médicales (26 %). La couverture d'assurance n'a modifié ni le traitement (97 %) ni les soins palliatifs (95 %) dans les régions où les soins n'étaient pas universels. L'expérience des médecins, la culture régionale et la formation de base ont eu un impact sur le traitement (toutes,  $p < 0,05$ ).

**Conclusion :** Malgré une concordance remarquable, des différences géographiques et des différences liées à la formation ont eu un impact sur le traitement et les soins palliatifs pour l'adénocarcinome de la tête du pancréas.

**P**ancreatic ductal adenocarcinoma (PDAC) is clearly among the most aggressive of all cancers.<sup>1</sup> This purports both depressing patient prognosis as well as frustrating experiences on the part of clinicians. The fact that the annual death rate approaches incidence speaks to the dismal natural history of this disease, as well as to limitations in our current treatment options. Despite significant improvements in surgical technique and perioperative care that have dramatically lowered 30-day mortality to less than 5% in high-volume centres,<sup>2</sup> end-of-life issues remain prevalent within this population.

In the context of PDAC, end-of-life concerns typically arise following either severe and immediate postoperative complications or delayed recurrence of the disease itself.<sup>1,2</sup> Providing appropriate and compassionate end-of-life care in the hospital setting can also be difficult for clinicians, as many of these patients die relatively late during their hospital course after undergoing highly sophisticated surgical and/or medical rescue therapies.<sup>3-6</sup> It is also clear that the psychological component of the patient-clinician relationship is fundamentally different from that between clinicians and patients who sustain major trauma or a catastrophic general surgical emergency. More specifically, patients with PDAC often enter the operating theatre with intact functional and mental status as well as a long-term relationship with their surgeons.

It is evident that end-of-life decision-making is an extremely complex and variable process on the part of both clinicians and family members.<sup>7-38</sup> It is best described as a nonlinear sequence that may include factors such as patient prognosis, predicted functional outcomes, personal beliefs, institutional resources, societal norms, personal experience and the rehabilitation and support network available upon discharge. Given the relative paucity of research focused on end-of-life care for patients with PDAC, the primary goal of this study was to better understand the end-of-life process following resection of head PDAC (pancreaticoduodenectomy) by highlighting the differences and similarities among clinician viewpoints from various countries and backgrounds.

## METHODS

We created a qualitative international survey outlining end-of-life issues for patients with head PDAC (see the Appendix, available at [canjsurg.ca](http://canjsurg.ca)). The authors of this 40-question survey consisted of hepato-pancreato-biliary (HPB) surgeons, specialists in intensive care medicine, bioethicists and rehabilitation therapists from various regions throughout the world (Canada, United States, Europe, Africa). It should be noted that this survey is an extension of similar work by authors within the trauma/critical care community.<sup>38</sup> Questions were created with the intent of characterizing the impact of medical, ethical, religious, social, training and system elements on end-of-life care for patients with PDAC in various geographic regions/countries. The study also

included specific scenarios for patients with nonresectable disease at the time of operative exploration. The survey was available for completion from Jul. 1 to Sept. 1, 2012, and was limited to HPB surgeons. Results were anonymous, and once completed they were sequentially forwarded to the authors in real time.

Advertisement of the survey to potential respondents was achieved via standardized email notifications to members of the Americas Hepato-Pancreato-Biliary Association (AHPBA), Canadian Hepato-Pancreato-Biliary Association (CHPBA), The Pancreas Club and to various members of other HPB-related societies. Each member was also asked to forward the survey link to additional surgical contacts with a potential interest in end-of-life care for patients with PDAC. Statistical analysis primarily involved frequency distributions.

## RESULTS

A total of 258 surveys were completed. Most respondents resided in the United States (40%), Canada (16%), Brazil (15%), the United Kingdom (8%), Germany (5%), South Africa (5%) and Mexico (4%). Additional survey respondents practised in Italy, the Netherlands, Norway, Finland, New Zealand, Australia, Argentina, Columbia and Japan. Most HPB surgeons (94%) worked in the country where they completed their HPB postgraduate training. While most clinicians believed that end-of-life decision-making varied significantly across countries (94%), few respondents had formal medical futility laws or guidelines (from local governmental bodies) to direct practice (26%).

### *Clinicians*

The respondents reported considerable experience in the management of head PDAC. Most surgeons (78%) were fellowship-trained in HPB surgery (39%), HPB transplantation (10%) or surgical oncology with HPB training elements (29%), and they had a mean of 16 (range 0-43) years' experience in university-affiliated teaching hospitals (93%). Most respondents also had at least 2 HPB colleagues at their institutions (solo 4%, 2 HPB surgeons 18%, 3 surgeons 18%, 4 surgeons 18%, more than 4 surgeons 42%). This pattern was not affected by country or culture.

Respondents reported significant diversity within their clinical practices. Few surgeons (33%) limited their practices to pure HPB diagnoses. The HPB surgeons typically and concurrently treated patients with gastrointestinal oncology (28%), general surgery (25%) or surgical oncology (14%) issues.

Reported religious beliefs (or lack thereof) were diverse among clinicians (Christian 58%, agnostic 17%, Jewish 8%, atheist 6%, Hindu 3%, Buddhist 3%). Both Canada and Europe had more respondents report agnosticism or atheism than any major religion. Respondents from the

United States were primarily Christian (87%). Most clinicians also believed their individual faith/religion did not influence the end-of-life care provided to their patients (92%). Many (71%) reported that their opinions and practices regarding end-of-life decisions/beliefs had changed with experience; only surgeons from Germany and Italy differed (67% in each country felt their beliefs had not changed over time). Most clinicians also felt their opinions regarding end-of-life care for patients with PDAC were in consistent agreement with those of colleagues at their institutions (89% infrequently or never differed). The need to transfer the care of a patient to a different physician/surgeon because of conflicts with the patient's family regarding end-of-life care was rare (6%). While agreement among respondents was similar overall, it is evident that surgeons with surgical oncology training reported significantly more frequent disagreement with colleagues at their institutions than either HPB- and/or HPB transplantation-trained surgeons (43% v. 6%, respectively,  $p < 0.001$ ).

### *Institutions*

Except in Canada, where 53% of end-of-life decisions in the intensive care unit (ICU) were directed by the critical care physician, the admitting surgeon (97%) typically retained control. Regardless of country, most institutions also offered ethics consultation services (93%). When ethics services were available, a minority of respondents used them (16%). When clinicians did use them, their interpreted utility ranged widely. More specifically, 40% of respondents found this service always or usually helpful. The remaining surgeons found it occasionally or never helpful (34%) or refused to use the service (25%). Although most respondents denied that patient insurance status impacted either treatment (97%) or palliation (95%) decision-making, 47% and 83% of surgeons in Brazil and South Africa, respectively, reported that resource limitations influenced their end-of-life decisions for patients with PDAC.

### *Preoperative preparation*

Most respondents considered pancreaticoduodenectomy for PDAC a potentially curative procedure (91%) and described it to patients as a "potentially curative operation with a high risk of tumor recurrence" (92%). Patient age alone was rarely (0.4%) considered to be the most important factor in deciding who was an appropriate candidate for resection. More specifically, age was defined as absolutely irrelevant among 54% of responders (40% considered age an important factor when the patient was older than 80 yr). Medical comorbidities alone were the dominant deciding factor for operative selection (79%).

The majority of surgeons, regardless of country, used routine preoperative multidisciplinary oncology conferences (94%) and medical/anesthesia assessments (68%) to

discuss patient issues of relevance. Only surgeons in resource-challenged environments (Brazil, South Africa) used medical/anesthesia assessments less commonly (21% and 33% respectively,  $p < 0.001$ ). Surgeons displayed varied use of routine consideration for neoadjuvant (chemo-radiotherapy) therapies (57%). This was clearly limited to resource-plentiful countries, but did not differ statistically among these regions (all  $p > 0.05$ ). Regardless of country, surgeons who defined themselves with surgical oncology training used routine neoadjuvant therapies more commonly than HPB-trained surgeons ( $p = 0.009$ ).

### *Operative technique and palliation*

Most surgeons (92%) considered resection and/or reconstruction of the portal vein an important part of their practice in achieving negative margins. In the operative setting, patients who were found to have hepatic metastases or peritoneal carcinomatosis with no preoperative gastric outlet or biliary obstruction were most commonly (85%) managed with nonsurgical approaches (biliary and duodenal stenting on demand). This differed significantly from the heterogeneity observed for patients with locally unresectable tumours who often (41%) received operative biliary and gastric bypasses (double bypass). Regardless of the rationale for unresectability, patients in South Africa (100%), Mexico (95%) and Brazil (91%) received significantly more surgical bypasses (all  $p < 0.05$ ). Concurrent chemical splanchnicectomy was also common (69%) across all countries.

### *Postoperative care*

Despite always or selectively admitting patients to the ICU following pancreaticoduodenectomy (33% and 25%, respectively), the use of preoperative critical care consultation across all respondents was low (21%). Respondents in the United States had the highest rate of routine postoperative ICU admission compared with Canada (78% v. 3%,  $p < 0.001$ ).

Severe postoperative complications following pancreaticoduodenectomy were most commonly (96%) treated with aggressive care, including cardiopulmonary resuscitation, intubation, transfer to the ICU and prolonged critical care admission if necessary. No respondent indicated a preference for comfort care only. The majority of surgeons also considered continuing critical care (ICU) for as long as necessary, with no specific time points to define futility (74%). Canadian and South African surgeons more frequently considered time-based end points for withdrawing care (57% and 50%, respectively,  $p = 0.005$ ). Canadian surgeons also reported more resistance (45%) from their intensivists regarding critical care admission and therapies for patients who underwent a pancreaticoduodenectomy than respondents in all other countries (9%,  $p = 0.004$ ).

Most surgeons followed their postoperative patients with scheduled outpatient visits in addition to radiological and

biochemical surveillance (74%). Others used outpatient visits with (15%) or without (11%) biochemical surveillance. Communication of specific values and data regarding the efficacy for adjuvant chemotherapy was also common (65%), with deferral to the medical oncologist being less frequent (29%). Canadian (53%) and Italian (100%) surgeons were most likely to defer these detailed discussions until the patient had met with a medical oncologist ( $p < 0.001$ ).

## DISCUSSION

Physician beliefs regarding end-of-life care vary by country and background as a result of a complex interaction between societal norms, religion, resources and technology.<sup>8,11-13,19-21,29,31-35,38-40</sup> Unfortunately, to our knowledge, this concept has not been explored in patients with head PDAC.

Unlike many explorations of end-of-life care among different subspecialties and etiologies, this survey of international HPB surgeons displays remarkable similarities across countries and regions. This finding differs significantly from a similar author-based study in the trauma/critical care field.<sup>38</sup> More specifically, very few of the observed differences were based on the country of practice. For example, the typical care algorithm of a patient with head PDAC would include interaction with an experienced, HPB-trained surgeon in an academic practice with plans for a curative resection. Surgical assessment of patient risk is based on medical comorbidities (not age) as well as a medical assessment clinic after discussion at a multidisciplinary oncology conference. Neoadjuvant therapy, portal vein resection/reconstruction and/or surgical palliation (including celiac plexus block) of locally advanced PDAC found intraoperatively is available. Severe postoperative complications are treated with aggressive rescue critical care of undefined duration, as guided by the admitting surgeon rather than by medical futility laws or assistance from ethics consultation services.

Although study respondents almost universally agreed that treatment of HPB-related neoplasms varied across countries (94%), most clinicians denied that their own individual faith influenced the end-of-life care they provided to patients. This contradicts the findings of a large European study that detected significant differences based on both doctor and patient religion.<sup>29</sup> Our study respondents' regions could be separated into 2 groups based on religion. While a statistical majority of respondents in Canada, Europe, Australia and New Zealand described themselves as agnostic, there were more religious cohorts in the United States, South Africa and Asia. This is consistent with the United States being one of the most religious nations in the developed world.<sup>41</sup> As would be expected with such a high level of experience among respondents, it was also clear that surgeon end-of-life care had changed with increasing clinical experience.

Despite this remarkable and extensive global agreement, notable differences mandate discussion. More specifically,

Canadian surgeons appear to represent outliers with regard to certain aspects of critical care. Canadians were much more likely to report intensivist-dictated (i.e., nonsurgeon) end-of-life decision-making as well as resistance regarding aspects of this care with their intensivist colleagues. This most likely reflects the reality that the majority of surgical critical care in Canada is provided by highly skilled nonsurgeon intensivists. Although Canada also displayed the lowest rate of routine postoperative ICU admission (3%), this friction may reflect a need to pursue more frequent preoperative critical care assessments and therefore communication. It may also provide an opportunity to discuss the reported use of defined, time-based end points for initiating withdrawal of care among Canadian patients. The explanation for such high postoperative ICU admissions in the United States (78%) likely reflects both the reality that these units are managed by surgeon-intensivists, as well as the importance of generating revenue in an open-market system.

It is interesting to note a clear association between resource-challenged regions (South Africa, Brazil, Mexico) and a higher rate of surgical bypasses (biliary and gastric) in cases of both locally unresectable and distantly metastatic tumours. This likely reflects limited access to postoperative endoscopic and/or percutaneous stenting techniques. It also clearly supports the self-reported impact of resource limitations on clinical and end-of-life decisions for HPB-related neoplasms within these countries.

The most intriguing heterogeneity among respondents surrounded differences based on the training fellowship of origin. More specifically, HPB surgeons who identified themselves as having completed a surgical oncology fellowship more commonly used neoadjuvant therapies for head PDAC than their colleagues who were trained as HPB or HPB-transplant surgeons. Although we cannot definitively identify the reason for this discrepancy, it may reflect (1) a closer faculty relationship with medical oncology and, as a result, greater use of multimodality therapies; (2) more frequent participation in preceding neoadjuvant trials and, therefore, greater support for their results; or (3) being partial to the greater emphasis on neoadjuvant therapies displayed at surgical oncology-based conferences. In addition to making up the smallest proportion of training paradigms, surgical oncologists also reported an increased rate of discordance with their colleagues regarding institutional treatment of PDAC. This observation is very interesting and may reflect differences in the perceived efficacy of neoadjuvant therapies, reasonable extent of surgical resection and/or reconstruction and/or the biology of disease itself. Surgical oncologists also displayed a lower rate of chemical splanchnicectomy in unresectable scenarios as well as a significantly higher rate of routine postoperative ICU admission. Further study is required to explain these observations.

On an institutional level, few respondents benefited from a medical futility law allowing them to proceed with

different end-of-life care than that desired by a patient's family. Unlike trauma or emergency surgery,<sup>38</sup> this is likely less of an issue in patients with PDAC given the outpatient opportunities to discuss goals of care and patient advance directives. It also provides an opportunity for detailed discussions of expectations and potential morbidity and mortality. This differs from many European regions<sup>11,19-21,34,35,40</sup> where doctor-family relationships are more paternalistic (only 17% to 44% of families are involved in end-of-life decision-making). It highlights the centrality of communication with family members and patients with regard to beliefs and values in North America.<sup>42</sup> Although some family members do not want to be involved in these decisions<sup>43</sup> despite patients' requests<sup>44</sup> and often display unstable preferences concurrent to an unwillingness to take responsibility for end-of-life decisions,<sup>30,45</sup> this perspective is supported by both regional ethical standards and legal liability issues.<sup>19,21,30,37</sup> It is also logical given the frequent disparity in opinions among physicians (< 10%), patients (40%) and families (32%) regarding their desire to use all available means to prolong life.<sup>19</sup> This reality is particularly interesting given the observation that the majority of HPB surgeons are willing to deliver invasive, costly and prolonged critical care in patients with severe complications and poor prognoses for 5-year survival. These viewpoints are clearly distinct from the more common acceptance of withholding and/or withdrawing therapies for terminally ill patients in Europe and Canada.<sup>7-37</sup>

### Limitations

Limitations of this study are primarily methodological. Because an Internet-based system was used to notify potential HPB surgeon responders, we were unable to determine a specific response rate. As a result, the accurate generalizability of this study is unknown.

### CONCLUSION

Although there are significant differences in religion, practice composition, training and institutional resources across the globe, there are also remarkable and more common similarities in end-of-life beliefs and practices among HPB surgeons caring for patients with head PDAC. The intersection of Canadian HPB surgeons with critical care in the context of severe postoperative complications appears unique. Surgical oncologists also display more common deviation from their colleagues. These differences require further study for improved explanation.

**Competing interests:** None declared.

**Contributors:** J.-F. Ouellet, E. Dixon, T.J. Howard and C.G. Ball designed the study. V. Hurdle, E. Dixon, F. Sutherland and C.G. Ball acquired the data, which E. Dixon, K. Lillemoe, C. Vollmer and C.G. Ball analyzed. E. Dixon, F. Sutherland and C.G. Ball wrote the article, which all authors reviewed and approved for publication.

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