PATTERNS OF CARE – IMPROVING EQUITY OF ACCESS TO OPTIMAL CARE

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Abstract

People diagnosed with pancreatic cancer suffer the worst five-year survival of any cancer. Resection of the primary tumour currently provides the only potential for cure. Increasing the proportion of patients who undergo surgical resection and ensuring that this occurs in a high-volume setting may lead to population-level survival gains. Access to chemotherapy in both adjuvant and palliative settings may lead to further improvements. Worse survival has been reported for patients from lower socio-economic and rural areas than those who are wealthier and living in major cities. Management in higher-volume hospitals tends to be associated with higher survival. Differences in patient factors such as age, performance status and the presence of co-morbidities may partly explain the survival discrepancies. However, international and limited Australian data suggest that not all patients receive optimal treatment, and that variability in care may be related to socio-demographic factors. There is considerable investment in identifying new strategies for diagnosis and treatment. However, immediate improvements could be made by implementing policies and procedures that enable all patients to be managed by high-performing multidisciplinary teams, ensuring receipt of optimal curative and supportive treatment modalities. This will also enable full realisation of benefits expected to accrue from the development of new treatments over the coming decades.

Pancreatic cancer is the tenth most commonly occurring cancer in Australia, affecting over 2700 people each year. It has the worst five-year survival of any cancer at less than 5%, so takes the lives of over 2500 Australians annually and is the fourth-leading cause of cancer death in both men and women.[1] There has been little change in the mortality to incidence ratio since the early 1980s, in contrast with a number of other cancers. As a result, it has been estimated that within the next decade it will become the second-leading cause of cancer death in the United States and this is likely also to be the case in Australia.[2]

The dismal prognosis in patients with pancreatic cancer is due firstly to the late stage at which most people are diagnosed. Consistent with international estimates,[3] almost 60% of pancreatic cancer patients in Australia are diagnosed with metastatic disease which precludes resection of the tumour.[4] A further 20-30% of patients have locally advanced disease and, although surgical techniques have improved, the vascular involvement is frequently too extensive to permit resection. The second reason for the poor survival has been the lack of efficacious systemic treatments. Until recently, administration of gemcitabine was considered the standard of care in both adjuvant and palliative settings, despite only small improvements in survival. The use of new regimens such as FOLFIRINOX and albumin-bound paclitaxel for treatment of inoperable pancreatic cancer, and increased investment in discovery of new therapies, may lead to further improvements in pancreatic cancer survival in the next decade.

Ensuring all patients receive optimal treatment will help to realise potential survival gains. However, international data suggests that patients from lower socioeconomic and rural areas may have worse survival than their counterparts from wealthier and metropolitan areas[5,6] and similar trends for geographic location have been observed in Australia.[7,8] While differences in patient factors such as age and the presence of co-morbidities may partly explain the survival discrepancies, it is likely that differential access to treatment also plays a role.

Increasing the proportion of patients who undergo resection of the primary tumour

Surgical resection of the primary tumour improves five-year survival from less than 5% to up to 20%,[9] but consistent with international estimates, only 15% of patients in two states of Australia underwent resection between 2009 and 2011.[4] Population-level survival estimates would improve if this proportion could be increased. It has been estimated that increasing the proportion of patients diagnosed with stage one and two (i.e. operable) disease from 6% to 19%, with a concomitant decrease in the proportion of patients with metastatic disease, would double five-year survival.[3]

Earlier diagnosis might increase the proportion of patients diagnosed with operable disease. Some studies,[10,11] although not all,[12] indicate that diagnostic delay is associated with later stage disease and poorer outcomes. However, a substantial component of the delay occurs as a result of the non-specific nature of symptoms which do not prompt early presentation to

medical practitioners, and it is unlikely that this will be amenable to significant improvement. Implementation of screening programs has more potential to lead to a shift in the distribution of the stage of disease at diagnosis, but considerable challenges remain. Population-wide screening is not feasible due to the relative rarity of pancreatic cancer. Indeed, modelling studies suggest that such an approach would reduce life expectancy due to false positive results and unnecessary surgery.[13] Screening is therefore currently restricted to people with genetic predisposition to pancreatic cancer and is only occurring within the context of research studies. Attempts to identify other subgroups of the population that have sufficiently high risk to make screening viable have so far proven unsuccessful.[14] Further, current screening relies on either computed tomography or magnetic resonance imaging; these are insufficiently accurate for identifying small tumours, may not be easily accessible and are expensive. Until these issues are resolved and screening becomes a feasible option, it is doubtful that there will be any discernible increase in the proportion of patients diagnosed with early stage, operable disease.

A second approach to increasing the proportion of patients who undergo surgery is to ensure that this treatment option is offered to all patients with resectable tumours and acceptable performance status. International data show that there is currently inequitable access to surgical intervention, with patients who are black, unmarried, have low education or socioeconomic status, and who come from rural rather than metropolitan areas being less likely to undergo resection of the primary tumour.[15-18] This is most probably associated with the expertise of the facility at which patients are staged. Patients who are managed at high volume or accredited cancer centres have higher likelihood of undergoing surgery than those who are treated at lower volume centres, and there is evidence that centralisation of care can increase resection rates.[19] There is limited published Australian information about patient factors such as education which might influence access to surgical treatment, but our unpublished data suggests that remoteness of residential location is inversely associated with resection, and a Queensland report shows a slightly higher resection proportion in more affluent patients with cancers of the pancreas, biliary tract and small intestine combined.[20] Guidelines suggest that all patients without metastatic disease should be assessed for tumour resectability by a multidisciplinary team that includes a specialist hepatobiliary surgeon;[21] developing referral pathways or telehealth facilities that enable implementation of this guideline has the potential to increase the number of patients in Australia that are offered a resection of their tumour.

Surgical volume and mortality/survival

Pancreatic cancer surgery is challenging due to the anatomic location of the pancreas, with its close proximity to large blood vessels into which the tumour has frequently invaded. The experience of the hospital at which patients are treated is therefore an important determinant of outcomes. A meta-analysis of 11 studies, most from the United States and none from Australia, found that patients treated in higher volume hospitals had lower post-operative mortality and longer overall survival.[22] The cut points for high and low volume varied markedly however, so volume is likely to be a marker of expertise and multidisciplinary care, but there is little evidence upon which to base recommendations about the minimum number of surgeries that should be performed. This is reflected in the guidelines which are inconsistent, with the National Comprehensive Cancer Network recommending a minimum of 15 surgeries per year, the National Cancer Institute Guidelines recommending five and the British Society of Gastroenterology not specifying a particular number. There are no specific Australian guidelines. Between 2005 and 2008 in New South Wales pancreatic cancer surgery took place at 37 hospitals. Only six of these performed more than six pancreatic cancer surgeries annually, and 15 (41%) undertook fewer than two procedures each year.[23] Between 2002 and 2011 in Queensland, 23 hospitals performed pancreaticoduodenectomies; by 2011 this number had dropped to 13[20] indicating that centralisation of care has been occurring in some jurisdictions.

Adjuvant chemotherapy

There is a high risk of recurrence after resection of the primary pancreatic tumour, with median disease-free survival of less than one year.[24] Clinical practice guidelines therefore recommend adjuvant chemotherapy or chemo-radiotherapy,[21] although the type of therapy to be used is not specified, probably due to a lack of consensus about the interpretation of clinical trial data. As with surgery, international evidence suggests variable implementation of adjuvant therapy. A recent report from the Netherlands found that only about half of patients received adjuvant chemotherapy, but this was higher in patients who underwent their resection at a high-volume hospital.[25] Similarly, studies from the United States found that receipt of adjuvant therapy was higher among patients treated at high volume hospitals (vs low volume) and at academic rather than community hospitals[15] and in white rather than black patients.[16] In Australia, chemotherapy with gemcitabine has been the standard of care, particularly since the publication of the CONKO-01 trial in 2007.[24] Presumably as a result of this key publication, use of adjuvant chemotherapy increased from 47% in Victorian patients diagnosed in 2002-2003 to 76% in patients from Queensland and New South Wales diagnosed almost a decade later. Patients who did not receive adjuvant treatment had worse performance status or a complicated post-operative course (unpublished data). This suggests that most Australian patients who undergo surgery are now receiving appropriate multi-modality postoperative care in accordance with guidelines.

Chemotherapy in advanced pancreatic cancer

The majority of patients present with metastases or locally advanced inoperable disease. For these patients there have been limited curative treatment options and symptom control has been the primary aim of management. In 1997, a landmark study was published which showed that, although gemcitabine resulted in only a modest survival benefit over 5-flurouracil, it delivered substantial improvements in pain, performance status and weight.[26] It subsequently became the standard of care for first line treatment in patients with advanced disease. As with surgery and adjuvant chemotherapy, there is evidence from the United States that socioeconomic disadvantage is associated with lower use of palliative chemotherapy.[16,27] Elderly patients with advanced cancer are also less likely to receive chemotherapy than younger patients, even though there is evidence of benefit in older patients.[28,29] In our population-based study in Queensland and New South Wales, only 43% of people diagnosed with inoperable disease received chemotherapy[4] but there are currently no recent published data about determinants of receipt of therapy. Newer chemotherapy regimens with greater impacts on survival and quality of life are now used for treatment of advanced pancreatic cancer, including FOLRIRINOX and albumin-bound paclitaxel and Gemcitabine.[30-32] Ensuring equitable access to these and other novel systemic treatments as they become available will be an important contributor to improvements in survival in the coming decade.

Conclusion

Pancreatic cancer continues to have unacceptably high mortality and patients report extremely high supportive care needs throughout the course of disease.[33] International and limited Australian data suggest that not all patients receive optimal treatment, and that variability in care may be related to socio-demographic factors. There is considerable investment in new strategies for diagnosis and treatment and there now appears to be light at the end of the tunnel. However, immediate improvements could be made by implementing policies and procedures that enable all patients to be managed by high-performing multidisciplinary teams, ensuring receipt of optimal curative and supportive treatment modalities. This will also enable full realisation of benefits expected to accrue from the development of new treatments over the coming decades.

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