Author’s response to reviews

Title: Variation in survival after surgery for peri-ampullary cancer in a regional cancer network

Authors:
Bassem Amr (dr_bassem277@yahoo.com)
Golnaz Shahtahmassebi (golnaz.shahtahmassebi@ntu.ac.uk)
Somaiah Aroori (s.aroori@nhs.net)
Matthew Bowles (matthewbowles@nhs.net)
Christopher Briggs (christopherbriggs@nhs.net)
David Stell (david.stell@nhs.net)

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Author’s response to reviews:

Dear Editor

Thank you for reviewing our submission and for forwarding helpful comments. We have made improvements to the paper, which are detailed below.

List of revisions

Reviewer #1:

1. The study appears to be looking only at patients who were offered to surgery. This however may not capture patients who had tumours and were not referred for surgery. Response: The study concept is to assess variation in the outcome of surgery for PC among patients from different hospitals and according to travel distance to the hospital. Patients who are not required to travel to the regional centre for surgery clearly cannot be disadvantaged. We did however assess the resection rate between hospitals, to identify potential under-referral of resectable cases. The resection rate was found to be similar between hospitals.

2. The authors state that they studied 394 patients who underwent surgery.

How many patients over the study period in the region developed pancreatic cancer and what percentage of these were the 394?
Response: The latest data available from the South West Cancer Network reports indicated that 1,318 new cases were diagnosed with pancreatic cancer within the cancer network between 2007-2011(1). Our studied population cohort represents about 11.3% of all diagnosed pancreatic cancer cases within the network.

Were there any differences in the rates of referral for surgery between the various hospitals?

Response: We have measured the operation rate in different hospitals (Table 1), and found a small difference. The referral rate is unknown as patients are filtered at a weekly audio-visual MDT, so that only operable cases are referred.

What was the incidence of pancreatic cancer in these drainage areas?

Response: Between 2007 and 2011 there were 1,318 recorded diagnoses of pancreatic cancer within the South West pancreatic cancer regional network. The annual incidence within the network is therefore 15.78 per 100000 population per year. The incidence within each hospital catchment area is unknown. But is likely to be similar.

What was the incidence of surgery for pancreatic cancer in district? This may indicate that there was indeed a failure to refer.

Response: The incidence of surgery varied over the duration of study within the regional cancer network. The published incidence of surgery for pancreatic cancer was 12.6%, 10.1%, 13.2%, 13% and 16.6% for consecutive years between 2007 and 2011(1). These figures are similar to other studies. As stated above we have good evidence that individual hospitals are not under-referring cases of pancreatic cancer as the resection rate in three of the referring hospitals is higher than that of the hospital hosting the regional HPB unit (Table 1).

3. Were all patients’ diagnoses with pancreatic cancer referred to a MDT for assessment as to suitability for surgery?

Response: An audio-visual ‘virtual’ MDT is held weekly with all referring hospitals in the Peninsula where patients with presumed diagnosis of PC are discussed. Potentially operable cases are then re-discussed at the Regional MDT in the HPB surgical centre (Hospital A). This has been made clearer in the Methods section.

4. Were the MDT at regional levels only or linked with the major centre?

Response: All patients were discussed at the regional MDT held at the regional HPB surgical centre (Hospital A). These MDT meetings were video linked with the referring hospitals within the catchment area. This has been made clear as stated above.

5. Were common protocols used for the staging of patients with pancreatic cancer. Response: The pathological stage of the primary peri-ampullary was determined according to Royal College of Pathology guidelines (2).
Were definitions of resectable, borderline resectable and irresectable agreed by all hospitals?

Response: The Royal College of Radiologists radiological staging system(3) was used by radiologists in all hospitals. This has been made clear in Methods section. There is however significant subjectivity in the interpretation of tumour resectability, which was resolved by discussion at the weekly audio-visual MDT, linked to the regional centre.

What proportions of patients had neo-adjuvant therapies from each centre?

Response: Six patients received neoadjuvant therapy prior to surgery. These were excluded from the study as the interval to surgery is greatly prolonged by treatment so that any potential effect of travel distance would be difficult to detect. This has been made clear in the Methods section.

6. The rate of laparotomy and no resection appears high at 31%.

What staging modalities were used pre operatively? And was this consistent for all cases?

Response: The non-resection rate of 31% is high by modern standards, but this series includes patients undergoing surgery more than 10 years ago. Furthermore the series has excluded patients undergoing surgery for adenomatous disease and other benign lesions, where the resection rate is near 100%. Pre-operative staging was undertaken by contrast-enhanced CT in all cases.

7. 61km was classified as the average distance travelled. For many countries such as Australia and NZ and Canada, this would be regarded as very close.

Could the authors comment on whether there is any data on distances this close and effects on outcomes

Response: There are no comparable data that we are aware from areas with greater travel distance for treatment. Our intention has been to demonstrate that it is possible to provide equity of access to treatment despite a relatively dispersed population. This may be harder to provide in the countries mentioned, and it would be interesting to see this data.

8. Many metropolitan regions have dense populations with infrastructure and transport limitations, whereas 60km in regional areas may be travelled far quicker than 20km in a city.

Did the authors consider measuring time of travel as being more relevant for the study?

Response: Although the time of travel within the cancer network is of interest, this was very difficult to measure due to variation in the mode of transportation and the status of the roads. Also within our network it is unlikely this issue will introduce bias, as there are no significant conurbations, and most travel is undertaken on relatively rural roads.

9. Almost all development of regionalisation has occurred with formal agreements and protocols for the investigation and treatment of patients to ensure seamless care no matter where the patient
presents in the network. To speak of regionalisation without implementing such a system is likely to result in the delays to treatment.

Would the authors like to comment on this?

Response: As suggested there are clear, agreed protocols within our network for the referral and treatment of patients. These are reviewed annually at a HPB Cancer Network meeting. This point has been added to the Introduction.

Was a comprehensive plan instituted to ensure seamless transfer of care and treatment between the smaller and larger centres?

Response: Within the Cancer Network and individual hospitals efficient transfer of care is ensured by specialist nursing and clerical staff whose role is to ensure smooth communication between centres. This has been made clear in the text as stated above.

10. Apart from the surgery itself, What proportion of treatment occurred in the regional centres?

Only surgery and immediate post-operative care is provided at the regional centre. This has been made clear in Methods section.

Was staging performed at the regional centres?

Response: Both radiological and pathological staging was undertaken at the regional centre. This has been made clear in Methods section.

Was adjuvant therapy given at the regional centre etc.

Response: Adjuvant therapy was provided by local hospitals. This is made clear in the Introduction.

The aim of regionalisation is for patients to receive as much of their therapy as close to home as possible with the support of the larger centre, and only have the most complex component at the larger centre. The philosophy of treatment here needs to be explained.

Response: This issue has been addressed by changes to the text noted above.

11. Many studies have shown that patients who present to smaller centres are less likely to be offered surgery, less likely to have palliative interventions and chemotherapy.

What were the outcomes for all patients in the area with pancreatic cancer, not just those who went to surgery?

Response: We do not have access to this information, and, though important, it is not relevant to our study question.
What was the percentage of patients who had adjuvant therapy after their surgery, or palliative therapy and did this differ between centres.

Response: We do not have access to this information. Although important, this question is not relevant to our study, which is to examine potential disadvantage caused by the need to travel to the regional centre for treatment. All adjuvant chemotherapy was provided in local hospitals, so patients were not disadvantaged by having to travel.

12. The list of references is limited in looking at socioeconomic and geographical isolation and the impact on outcomes and whether this can be overcome by a protocolised networked system as part of centralisation of surgery for low volume oncology. Numerous publications have recently been published from Australia, Canada, New Zealand and Scandinavia. Would suggest that these be referenced in the discussion

Response: Although there are many other publications relating to the influence of socioeconomic factors in the outcome of pancreatic surgery we haven’t been able to identify a large body of work addressing the specific issue of the effect of geographic isolation within a cancer network on outcomes.

Reviewer 2#:

Dr. Amr and colleagues have submitted a manuscript investigating the impact of regionalization on survival for patients with periampullary cancers. This important study provides some insight in the impact of consolidating pancreatic surgery. This study confirms findings reported in the United States that regionalization has improved outcomes. The manuscript is well written and I have few concerns.

I would recommend the findings noted using bullet points in the discussion be present as separate table or written in paragraph form.

Response: This has been changed as recommended.

References


Pancreas. 2104.