

I had the opportunity of working with Professor Hemant Kocher's group at Bart's Cancer Institute for a few years now and have published two articles with them. The group focuses on hepato-pancreato-biliary cancer. The elective was just about the right time to embark upon another project with them and learn new things from this opportunity.

We are currently looking at the factors that may offer prognostication of patients with unresectable pancreatic cancer undergoing double bypass (hepaticojejunostomy and gastroenterostomy). Four objectives of my elective are:

1. Finding a correlation between different palliative interventions and symptom control
2. Finding a set of criteria to identify patients who would benefit from palliative interventions
3. Looking at the translatability of the finding of previous research in this particular area of oncology to the clinical setting in various countries including the UK
4. I am especially looking to learn how to be a first author

Despite rigorous research and recent therapeutic advancements, pancreatic cancer remains exceedingly lethal. Median survival ranges from approximately 11 months in pancreatic cancer with metastases to between 26 months in patient whose disease is resectable and receive neo-adjuvant or adjuvant therapy. Primary treatment is resection with curative intent. However, it is not always possible in majority of patients as a significant proportion of the patients (up to 80%) have metastases or locally advanced disease by the time the diagnosis is made. Therefore, curative intent surgery is commonly non-feasible and palliative therapy is often favoured instead. In addition, despite preoperative staging modalities, between 4% and 13% of pancreatic cancer patients are found to be unresectable at surgical exploration.

Biliary and gastric outlet obstruction are common complications in locally advanced disease and palliative interventions offered include hepaticojejunostomy, gastroenterostomy, double bypass, coeliac plexus blockade or stent insertion via ERCP or PTC. Different procedure carries different risks and benefits. Different patient has different suitability in terms of which procedure is deemed best for their symptom control. In addition, for a number of years, the decision of which procedure to undertake has been dependant on the clinical experience of the surgeons although more studies evaluating different palliative

procedures and looking at a set of criteria to identify suitable patients for these procedures have been published.

As for biliary obstruction, common symptoms include obstructive jaundice, pruritus, fat malabsorption, diarrhoea, and cachexia. Endoscopic interventions have become extensively available to overcome biliary obstruction. ERCP with stent placements is commonly offered to patients with locally advanced or metastatic pancreatic cancer. Advances in this area have resulted in successful procedure in more than 90% patients with equal efficacy when compared to surgical palliation. In addition, the discovery of self-expanding metal stents with low axial force and flared ends have overcome past issues such as stent migration or tumour ingrowth. However, this procedure is not without any side effects. This procedure is associated with recurrent jaundice, cholangitis and acute pancreatitis which require re-interventions. Endoscopic technique with stent placement to manage gastric outlet obstruction has also been offered. In comparison to gastrojejunostomy, stented patients had fewer complications, quicker return to oral intake and shorter hospital stay. Complications, however, may occur in up to 12% of the case and include perforation, aspiration pneumonia and stent migration.

In the case of repeated complications, biliary- or gastro-enteric bypass, or even double bypass may be preferred. If performed prophylactically in asymptomatic patients, bypass procedures have been shown to result in low complication rates and sustainable palliation. However, the conundrum is that performing these operations on symptomatic patients with advanced disease commonly result in operative complications and poor quality of life. Complication and mortality rates in the patient undergoing laparotomy plus a palliative procedure were found to be 28.0% and 2% respectively. Therefore, identifying prognostic factors that predict the complications occurring is therefore of beneficial.

While a substantial number of studies have tried to find prognostic factors for survival in patients with advanced pancreatic cancer receiving palliative chemotherapy but studies attempting to look at prognostic factors specifically in patients undergoing double bypass surgery are still limited. Some independent negative prognostic factors include performance status (PS), the presence of distant metastatic disease, the status of initially unresectable disease, carcinoembryonic antigen (CEA) level, carbohydrate antigen 19-9 (CEA19-9) level, and neutrophil-lymphocyte ratio (NLR). However, whether these factors are also applicable in prognostication of patients undergoing double bypass procedure still remain unknown. In practice, the decision to perform endoscopic or operative palliation depends largely on life expectancy, performance status and incidence of recurrent

symptoms following less-invasive endoscopic palliation. Many surgeons would advocate for operative intervention to be offered to patient whose life expectancy is at least 4 months and with a good functional status.

In our study, we have been looking at whether the aforementioned biomarkers and other potential factors would offer reliable prognostication in these patients. We included peri-operative haemoglobin, total white cell count, lymphocyte, neutrophil, CRP, albumin and CA 19-9 as well as functional status and histology as potential negative prognostic marker. We endeavour to find correlation between these and patients' survival following double bypass surgery.

As mentioned above, even with the state-of-the-art computed tomography (CT), between 4% and 13% of patients with pancreatic cancer are found to have locally advanced disease at exploratory laparotomy, rendering their cancer unresectable. A palliative approach is normally offered to these patients. Due to the lack of clear-cut point as to which patient gets which treatment and when, different institution employs different patient criteria for different palliative procedure. Some hospitals prefer to do surgical bypass on patients who are fit for surgery, found to be inoperable at laparotomy and have a reasonable prognosis and reserve stenting techniques for those with a short life expectancy. Other hospitals however, the approach has been to treat only symptomatic patients at the time of laparotomy and leave interventions (endoscopic or operative procedures) until when symptoms occur in the remaining patients (wait and see strategy).

Prior to this project, I was involved in two projects, both of which were oncology-related clinical studies. I had to extract relevant information of hundreds of patients from hospital database. The data were subsequently analysed by my second supervisors who was one of the PhD students in the research group. He managed to publish the two projects and I was listed as the second author. Following these publications, I was suggested by him to make an attempt to be a first author. He mentioned this current project (on prognostication of terminal pancreatic cancer patients following double bypass) to me and believed that it would make a good publication since currently there is only a limited number of studies specifically looking at the subject. It was daunting to decide to agree with his suggestions but he reassured me that they would help me along the way.

The biggest hurdle to me was to get things started. Fortunately, after the first meeting with Professor Kocher and my second supervisor (who was working in Italy), I had a better idea

of what to do to kickstart this project. We discussed about the overview of the project, registering it, construction of the data spreadsheet and subsequently looked into the details regarding various potential prognostic factors to consider. In addition, I also arranged a meeting with another PhD student in the group to get extra feedback on the study design. This highlighted the importance of teamwork and teaching within the team. Moreover, it was a unique learning experience to work with people in different countries.

Being a first author also involved a lot more background reading as I had to be updated with how the research on this particular topic has progressed. In addition, I had to familiarise myself with concise academic writing style.

Another challenge that came up was the cyber-attack that affected NHS computers including that within Barts Health. Considering that the patients included in the study are patients treated at Royal London Hospital, the project was unfortunately stuck for a few weeks. I could not proceed with data compilation so used the time to do more background reading and write the introduction instead. Upon reflection, this unprecedented incident may commonly occur during research project. It put me under a bit of stress but this experience taught me to not dwell on the stress and focus on what could be done instead. Due to this incident, I have not managed to finish data compilation as of now. However, I will try my best to allocate some days/afternoons off including weekends to hopefully finish extracting the data on time. Time prioritisation can be tricky but this is yet another challenge that I will have to overcome as it is likely that in the future, I would have to juggle work on the ward/in the clinic with academic commitment.