## **Editorial/Commentary**

Hyaluronate carboxymethylcellulose-based bioresorbable membrane facilitates a two-stage pancreaticoduodenectomy: unnecessarily necessary?

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**Running Head:** Hyaluronate carboxymethylcellulose membrane and two-stage pancreaticoduodenectomy

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Yamazaki and colleagues [1] have presented an interesting retrospective cohort study on the safety and feasibility of the use of a hyaluronate carboxymethylcellulose (HCM)-based bioresorbable membrane to reduce adhesions at the second stage of a two-stage pancreaticoduodenectomy performed 4 to 8 weeks after the initial resection. The authors have reported reduced adhesions, thereby facilitating the second-stage reconstruction.

There was also formation of good granulation tissue around the exteriorized pancreatic fistula despite the presence of the HCM-based membrane. The authors used operative duration and blood loss at the second stage as markers for the efficacy of the HCM-based membrane, but found no difference between the HCM-based membrane group (n=61) and the historical control group in which the HCM-based membrane was not used (n=145) in the rate of pancreatic fistula formation.

Although the efficacy of HCM-based membranes in reducing intra-abdominal adhesions after surgery is well established [2], there are no previous reports on their use in two-stage pancreatic surgery. However, this study [1] is limited by the inherent bias associated with retrospective cohort studies. Additionally, it is restricted by the fact that a two-stage pancreaticoduodenectomy for cancer is not standard procedure across the vast majority of centres outside Japan. The two-stage procedure with planned readmission was directed towards patients at high-risk for a pancreatic anastomotic leak and the authors demonstrate an excellent 0% mortality, albeit with much longer hospital stays than seen in other centres.

There are several issues related to the study [1]. Although a two-stage pancreaticoduodenectomy may be justified in certain situations, such as damage-limitation surgery for pancreatic trauma [3], the drawbacks of the procedure have been highlighted

previously [4] and include increased morbidity, barriers to the delivery of adjuvant therapy, and a negative impact on both health economics and quality-of life. It is remarkable that the vast majority of procedures performed in this study [1] were two-stage operations [213 (87.3%) two-stage *versus* 31 (12.7%) single-stage over 7 years]. It is difficult to reconcile this with the contention that two-stage procedures were performed only for patients deemed to be at high-risk of pancreatic leak. The authors did not perform an assessment of the risk of pancreatic leak using scoring systems to inform this decision. Cumulatively, the complication rate across the two-stage procedures was higher than rates for a single stage procedure when compared with the majority of high-volume pancreatic centres [5]. The additional comorbid burden placed by a second procedure with an iatrogenic external fistula as well as the obstacle this would place in the provision of adjuvant chemotherapy and the negative impact on the individual patient's quality of life complicates the picture. It is also important to note that seven patients were excluded from the analysis because the second operation was not performed for a variety of reasons that included disease progression (n=5), cerebral infarction (n=1) and patient refusal (n=1).

While we appreciate that the use of the HCM-based membrane reduced adhesions at the second stage, it is difficult to rationalise how the presence of the HCM-based membrane would reduce adhesions on one hand and promote good external fistulisation with granulation tissue formation on the other. As a marker of ease of second stage laparotomy, the reduction in blood loss in the HCM-based membrane group compared with the control group, although statistically significant, was clinically negligible (36 vs. 58 ml). There was a longer operative duration in the control group than in the HCM-based membrane group (151 vs. 105 min) for the second stage operation. However, it is difficult to envisage how the

second stage reconstruction could have been performed at the lower limit of the quoted range of the operative duration of 30 minutes in both groups. Nevertheless, despite concerns about the need for a two-stage pancreaticoduodenectomy, this study is useful in demonstrating that HCM-based membranes can be used safely in patients who undergo this procedure.



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