Classical or pylorus-preserving pancreatoduodenectomy in pancreatic and periampullary cancer: "The jury is still out!"

Hüttner *et al.*[1] present an update of their previous Cochrane review[2] comparing pylorus-preserving pancreaticoduodenectomy (pylorus-preserving Whipple [PPW]) versus classical pancreaticoduodenectomy (classic Whipple [CW]) for surgical treatment of periampullary and pancreatic carcinoma. The updated review included two new trials[3,4] published since the last version taking the tally of included trials to eight overall.[3-11] The present review,[1] similar to the previous one,[2] looked at the primary outcomes including pancreatic fistula, delayed gastric emptying (DGE), and biliary leak rates, secondary outcomes such as survival and postoperative mortality, and perioperative parameters such as intraoperative blood loss, red blood cell transfusion, operating time, postoperative bleeding, wound infection, pulmonary complications, necessity for re-operation, duration of hospital stay, quality of life, and status of resection margin.

Table 1 compares the various outcomes analyzed in the two manuscripts. The findings of the updated review largely echo the previous results, namely, there exists no difference between the CW and PPW in terms of overall morbidity, mortality, and survival. However, a novel finding in the updated version is the significantly increased risk of DGE in patients undergoing a PPW. On the flipside, PPW has been consistently shown to be associated with shorter operating times, lower intraoperative blood loss, and hence, a reduced need for blood transfusion.

As was lucidly stated by the authors in the discussion, the analysis does reveal problems related to heterogeneity between the studies, variation in definitions used within the trials as well as the process of randomization. Even the intention-to-treat analysis was specified in only one trial.[10] Also, not considered in the analysis are the data on whether the patients received neoadjuvant or adjuvant therapy – a significant determinant or morbidity, mortality, and survival.

Despite its inherent shortcomings, this manuscript represents the most updated review published on the topic and provides a "real world" overview of the differences (or lack of them) between the procedures for the management of pancreatic and periampullary cancers considering that the authors in the Collaboration with the Cochrane system have conducted an analysis reducing the influence of bias and heterogeneity as best they could.

However, this review certainly provides sufficient justification for a large randomized controlled trial investigating CW and PPW in pancreatic and periampullary cancers to more conclusively answer this question.

Table 1: Comparison of the outcomes analyzed between the two studies

Outcome	Diener *et al.*, 2014[2]			Hüttner *et al.*, 2016[1]		
	Number of studies	Effect size	Inference	Number of studies	Effect size	Inference
Primary outcome						
Pancreatic fistula	5	OR 0.86 (0.41, 1.81)	No difference	7	OR 0.95 (0.49, 1.84)	No difference
Delayed gastric emptying	5	OR 2.35 (0.72, 7.61)	No difference owing to heterogeneity	7	OR 3.03 (1.05, 8.70)	Favored CW
Biliary leak	3	OR 1.35 (0.10, 18.55)	No difference	5	OR 0.96 (0.15, 6.17)	No difference
Secondary outcome						
Survival	3	HR 0.84 (0.61, 1.16)	No difference	3	HR 0.84 (0.61, 1.16)	No difference
Postoperative mortality	5	OR 0.49 (0.17, 1.40)	No difference	7	OR 0.64 (0.26, 1.54)	No difference
Perioperative parameters						
Intraoperative blood loss	1	MD –0.76 (–0.96, –0.56)	Favors PPW	5	MD –0.32 (–0.62, –0.03)	Favors PPW
Red blood cell transfusion	2	MD –0.65 (–1.92, 0.61)	No difference	5	MD –0.47 (–0.86, –0.07)	Favors PPW
Operating time	3	MD –68.26 (–105.70, –30.83)	Favors PPW	7	MD –45.22 (–74.67, –15.78)	Favors PPW
Postoperative bleeding	3	OR 0.74 (0.29, 1.88)	No difference	5	OR 0.74 (0.32, 1.74)	No difference
Wound infection	4	OR 0.85 (0.35, 2.05)	No difference	4	OR 0.85 (0.35, 2.05)	No difference
Pulmonary complications	3	OR 0.67 (0.29, 1.58)	No difference	3	OR 0.67 (0.29, 1.58)	No difference
Necessity for re-operation	2	OR 0.82 (0.38, 1.75)	No difference	3	OR 0.80 (0.38, 1.68)	No difference
Duration of hospital stay	1	MD –1.80 (–8.94, 5.34)	No difference	5	MD 0.26 (–2.04, 2.56)	No difference
Status of Ro resection margin	-	-	No difference	4	OR 0.92 (0.39, 2.15)	No difference

OR – Odds ratio; HR – Hazard ratio; MD – Mean difference; CW – Classical Whipple; PPW – Pylorus-preserving Whipple

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