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## **Systematische Übersichtsarbeit zum Vergleich der pyloruserhaltenden gegenüber der klassischen Whipple Operation**

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Pancreatic cancer is the fourth leading cause of cancer death for men and the fifth for women in the United States. It is a highly malignant disease although the adjuvant and surgical treatment options have improved in the last decades.

Two operations are mainly performed to remove the affected part of the pancreas: the classical Whipple operation and the pylorus-preserving Whipple operation.

Due to different trial results about side effects and oncological adequacy it is unclear which method is to prefer. Therefore, this systematic review and meta-analysis aims to summarize the existing evidence on effectiveness of PPW and CW for treatment of pancreatic cancer.

The systematic review was written according to guidelines published by the Cochrane Collaboration and the MOOSE and QUOROM statement.

A systematic search of the databases MEDLINE, EMBASE and The Cochrane Library revealed 4503 citations. Forty-three studies (six RCTs, 12 prospective and 25 retrospective trials) representing 3893 patients were included in the meta-analysis. The included RCTs as well as the observational studies were heterogeneous in terms of quality, methodology, patient characteristics and investigated outcomes.

Perioperative parameters were only analyzed from RCTs and demonstrated a significant reduction of operating time [min] for the PPW (WMD -68.26; 95% CI -105.7 to -30.83; P=0.0004). Intra-operative blood loss [l] was significantly reduced in the PPW group (WMD -0.76; 95% CI -0.96 to -0.56; P<0.00001). No difference could be found in the analysis of units of blood replacement used (WMD -0.65; 95% CI -1.92 to 0.61; P=0.31).

No statistically significant difference in postoperative mortality could be found between the classical Whipple operation and the pylorus-preserving Whipple operation (RCTs: HR 0.49;

95% CI 0.17 to 1.4; P=0.18; prospective cohort studies: HR 0.63; 95% CI 0.34 to 1.18; P=0.15; retrospective cohort studies: HR 0.7; 95% CI 0.37 to 1.31; P=0.27).

Postoperative morbidity was not statistically different between both procedures. The occurrence of delayed gastric emptying was not significantly different (OR 2.35; 95% CI 0.72 to 7.61; P=0.16) but the heterogeneity of the summarized results was high ( $I^2$  test 75.6%). No significant differences could be seen in the occurrence of biliary leakage (BL), postoperative bleeding (PB) or wound infections (WI) either (BL: OR 1.35; 95% CI 0.1 to 18.55; P=0.82; PB: OR 0.74; 95% CI 0.29 to 1.88; p=0.53; WI: OR 0.85; 95% CI 0.35 to 2.05; P=0.72). Pancreatic fistulas (PF) and pulmonary complications (PC) do not seem to occur significantly more often after one of the procedures (PF: OR 0.86; 95% CI 0.41 to 1.81; P=0.68; PC: OR 0.67; 95% CI 0.29 to 1.58; P=0.36) and the rate of reoperations was not statistically different between the two operations (OR 0.82; 95% CI 0.38 to 1.75; P=0.6). Length of hospital stay [days] showed similar results in both groups (WMD -1.80; 95% CI -8.94 to -5.34; P=0.62).

It was impossible to pool data from the outcome 'quality of life' quantitatively but the qualitative summary revealed no difference in most of the analyzed sub-issues or an advantage for the pylorus-preserving Whipple operation.

The analysis of survival did not reveal any differences between both procedures. The pooled hazard ratio for RCTs was 0.8 (95% CI 0.53 to 1.22; P=0.31), it was 0.84 for prospective cohort studies (95% CI 0.84 to 1.0; P=0.05) and 0.84 for retrospective cohort studies (95% CI 0.7 to 1.01; P=0.06).

The results of these analyses have to be regarded with caution since there was heterogeneous methodological quality of included trials. There is as well evidence for publication bias and it might be that some small studies in favor of the CW operation are missing in the meta-analysis.

More research is needed to explore the quality of life after both procedures. One of the most important factors in this field is to strengthen the need for the use of a standardized instrument to assess quality of life since this ensures comparability.

It can be concluded, that the available evidence does support a difference in the comparison between the pylorus-preserving Whipple operation and the classical Whipple procedure in terms of blood loss and operation time but future research is needed to prove these findings and investigate differences in outcomes with less existing evidence like quality of life.