Is pace the key to success when exploring the ALPPS?

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Background & Aim:
The optimal inter-stage interval for ALPPS has not yet been defined, with most proponents suggesting a rapid second stage within 6 to 10 days as the key to success compared to classical 4-8 weeks for two stage liver resection. However, without accurate volumetric and functional future liver remnant (FLR) assessment, this is a high-risk strategy associated with high morbidity and mortality, which has discouraged uptake of ALPPS in new centres. In this analysis we aimed to investigate the impact of delaying the second stage (inter-stage interval ≥ 14 days, d-ALPPS) in the treatment algorithm of colorectal liver metastases (CRLM) in comparison to ALPPS (inter-stage interval<14 days) to determine if d-ALPPS is a safe option for centres with no access to volumetric and functional FLR analysis.

Study Design:
A prospective multi centric analysis was performed, including consecutive patients ≥ 18 years undergoing ALPPS (inter-stage interval < 14 days, n=19) and d-ALPPS (inter-stage interval ≥ 14 days, n=19) for CRLM between January 2013 and December 2018. The two cohorts were propensity score matched. The primary endpoints focused on onco-surgical outcomes including R0 resection, completion rate and one year survival rates. Secondary endpoints were morbidity and mortality.

Statistical Analysis:
We used propensity score matching to reduce differences in confounding variables between the groups being compared. Matching variables were age, sex and synchronous/metachronous disease. The cohorts were matched 1:1. Standardised differences were used to assess balance between groups. We compared outcomes using the Z-test for comparing proportions with a p-value of 0.05 being considered statistically significant.

Results:
There were no significant differences with respect to age, sex or synchronous/metachronous CRLM between the two matched cohorts. The median inter-stage interval was 8 days (range 7-10 days) in the ALPPS group compared to 14 days (range 14-84 days) in the d-ALPPS group. There were 11 (58%) postoperative complications in the ALPPS group compared to 7 (37%) complications in the d-ALPPS group (p=0.2). Assessing complications > Clavien-Dindo 3, this difference was not significant among the two groups (16% (3; 3xCD3b) vs. 11% (2;1xCD3b,1xCD5); p=0.6). There were no significant differences in terms of onco-surgical outcomes for both groups. The one-year survival rates were 89% for the ALPPS group and 74% for the d-ALPPS group, (p=0.2). There was no difference in the R0 resection rate between the groups (95% ALPPS vs. 100% d-ALPPS; p=0.7)

Results:
Until recently, ALPPS has been associated with high rates of peri-operative morbidity and mortality. This analysis has shown that this operation has now evolved to a level comparable to more classical liver resection approaches; both ALPPS and d-ALPPS were found to be safe options.

Conclusions:
This analysis suggests that d-ALPPS is a safe method, even in new centres without access to preoperative volumetric and functional assessment without compromising onco-surgical outcomes by delaying the second stage of the operation. d-ALPPS should be accepted as a valuable and safe new treatment alternative to ALPPS for both new and established liver centres.