

Center variation in adverse post-operative outcomes following associating liver partition and portal vein ligation for staged hepatectomy (ALPPS)

Background

Considerable hospital variation in clinical outcomes has been observed following a variety of operations, ranging in surgical complexity from appendectomy to complex thoracic and hepatobiliary surgery¹⁻⁷. But much of the literature evaluating hospital level variation has focused on the inverse effect of hospital volume on perioperative complications and mortality⁸⁻¹¹ and less work has been dedicated to describing the overall variation in adverse perioperative outcomes due to the effect of treatment center.

Associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) is a relatively new hepatobiliary innovation which has generated considerably controversy over the past decade¹². Compared to conventional two-staged hepatectomy for extensive bilobar or central colorectal liver metastases, ALPPS increases the feasibility of second-stage hepatectomy completion at the cost of higher perioperative morbidity and mortality^{13,14}. But, in single and multicenter case series, institutions have reported a wide range of morbidity and mortality estimates following ALPPS¹⁵⁻²⁴. Further, improvements in perioperative outcomes have been observed over time due to selection of younger patients, fewer patients with biliary tumors, and patients with more favorable functional status²⁵. This trend in improved outcomes may also be due to a center and surgeon learning curve, which has been described for other complex hepatobiliary operations²⁶⁻²⁸.

We have previously hypothesized that there is substantial variation in ALPPS outcome across centers, even after accounting for differences in surgical volume. Similarly, there may also be variation in the rate at which center-specific outcomes improve over time. Neither of these aspects of center variation has been previously studied and while the purpose of this study is not to identify any specific underpowering centers, we will clarify whether the poor outcomes reported in a number of prior studies are center-specific or if they are generalizable to all centers performing ALPPS.

Objectives

The purpose of this study is not to identify the performance of any specific centers, and centers will be de-identified for data analysis. Our objectives are to understand the extent to which overall center variation explains the variation reported in ALPPS outcomes. Specifically, we aim to:

1. To estimate the center-level variation in perioperative outcomes (severe morbidity defined as Clavien-Dindo 3b or greater, and 90-day mortality) following ALPPS for colorectal liver metastases
2. To estimate residual center-level variation in perioperative outcomes after accounting for differences in patient, surgical technique, and surgical volume factors.
3. To estimate the center-level variation in the effect of time on perioperative outcomes following ALPPS

Methods

Primary outcome

Severe post-operative morbidity defined as Clavien-Dindo 3b or greater.

Secondary outcomes

90-day mortality and major post-operative morbidity, defined as Clavien-Dindo 3a or greater.

Co-variates

De-identified center/hospital identifier, year of surgery, patient age, patient co-morbidities and functional status, pre-treatment characteristics (receipt of neoadjuvant chemotherapy, number of cycles), treatment characteristics (type of ALPPS, synchronous colorectal resection), center/hospital volume.

Statistical analysis

A Bayesian hierarchical multivariate modelling approach will be used to estimate the posterior distribution of the risk of the primary and secondary outcomes, with adjustment for patient and center level variables, and clustering at the center/hospital level.

Impact of the findings

In the context of the ongoing controversy regarding ALPPS for patients with extensive colorectal liver metastases, assessing the presence of considerable center-level variation is important in order to inform recommendations. We hypothesize the existence of high-performing centers, independent of operative volume, at which ALPPS can be applied with less perioperative risk than at lower-performing centers. Further, we will describe the extent to which improvements in ALPPS outcomes over time are observed at various centers. For instance, we will evaluate whether initially underperforming centers experience a steeper, and more rewarding learning curve than initially high performing centers. These findings may be generalizable to other complex hepatobiliary operations.

Cover letter to the Scientific Committee

Dear Profs Lodge, Schnitzbauer, Rogiers, Barkun, Machado, Abdalla, Kukudo, and Petrowsky,

We propose an analysis of the ALPPS registry aimed at assessing center-level variation in perioperative outcomes following ALPPS for colorectal liver metastases. Centers will be completely de-identified in the analysis and publication. Our analysis will help to inform the current discussion about the role of ALPPS by demonstrating whether high-performing centers are able to apply the technique with considerably greater safety compared to lower-performing centers. Further, we hope to shed light on center-level variation in the learning curve in complex hepatobiliary surgery.

We confirm that the ALPPS Registry Data will be analysed only for the above protocol and will not be used to address other research questions. We have read, and agree with, the Statutes of the ALPPS Registry as well as the publication policy.

Sincerely,

Kerollos Nashat Wanis

Roberto Hernandez-Alejandro

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