

# How should mortality after ALPPS be reported? Results of a novel hazard threshold estimation method

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## Background

Mortality after liver resection in studies is reported as in-hospital mortality, 30-day mortality or 90-day mortality. Recent studies (Mise et al., *Ann Surg* 2015;262(6):1071-8; Schiergens et al., *Surgery* 2015;158(6):1530-7) suggest that the 90-day mortality reflects the statistical acute postoperative period (sAPP) after liver resection better, and that in contrast 30-day mortality or in-house mortality leads to underreporting and bias. To determine sAPP in an objective manner, we developed a novel statistical method of hazard threshold estimation. This method allows a statistical definition of the sAPP with a confidence interval (Schiergens et al. *Surgery* 2015;158(6):1530-7). The sAPP following ALPPS has not been investigated in detail. We studied the 90-day mortality after ALPPS for hepatocellular carcinoma (HCC) in the ALPPS registry and compared it to ALPPS for colorectal liver metastases, and we found it to be almost fivefold higher than for colorectal liver metastases (CRLM; 31 vs. 7 %; D'Haese et al., *Ann Surg Oncol.* 2015). It is not entirely clear if 90-day mortality should be the reporting standard for two-stage hepatectomies just like for simple hepatectomies and what should be the confidence interval. Additionally it is not clear if the 90-day postoperative period should be counted after stage 1 or after stage 2. These different ways to assess mortality after ALPPS could be objectively validated using our new methodology.

## Objectives

The aim of the study is to statistically calculate the sAPP after ALPPS by applying our novel method of threshold estimation to the postoperative daily hazard rate. Additionally we would like to perform a multivariate analysis of several covariates as potential risk factors for the methodologically exact mortality periods.

## Methods

As described above, a novel statistical method of threshold estimation based on data of Malik et al. (please see Schiergens et al., *Surgery* 2015;158(6):1530-7 for details) will be applied to the daily hazard rate to determine the sAPP. Multivariate analysis will be performed using standard Cox models and novel extended regression models such as the Cox-Aalen model (Schiergens et al., *Liver Int* 2016).

## Impact of the findings

The findings of this analysis would indicate which mortality period to report and to analyze after ALPPS.