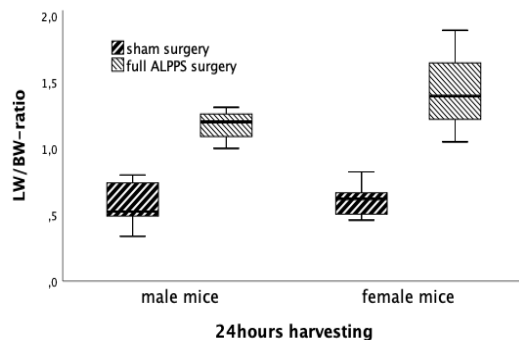


## Identification of gender differences in patients undergoing ALPPS - Do female livers regenerate faster?

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**Background:** Few experimental studies have suggested gender disparities in the regenerative ability of the liver.(1-4) Available evidence suggests that female rodents regenerate significantly better after major hepatectomy compared to their male counterparts; an effect possibly attributable to the female hormone estradiol (2, 5).



Our preliminary findings in mice have confirmed an improved regenerative response in females after ALPPS surgery. To our knowledge, data to confirm these findings in human are lacking. Given that regeneration is accelerated after ALPPS,(6, 7) gender differences in the rate of liver growth may be prominent. Therefore, the ALPPS registry offers a unique opportunity to explore sex-dependent disparities in human regeneration as well as in associated post-operative morbidity/mortality.

**Objective:** The aim of this study is to identify gender differences in ALPPS-induced liver regeneration, in post-operative liver failure, and in the whole post-operative course. Primary endpoints are clinical measures of liver regeneration (i.e. static and dynamic volumetric parameters, liver function and failure) stratified by gender, tumor entity/load, and associated treatment. Secondary outcome measures include morbidity, mortality, and long-term outcome.

**Methods:** The international ALPPS registry will be screened separately for pre- and postmenopausal female cases matched to males by age, background disease, tumor type/extent, and treatment. First, a univariate analysis will be performed to screen for gender differences in the respective groups. Second, a multivariate analysis will be carried out to identify predictors of improved regeneration.

**Relevance:** This, to our knowledge, is the first clinical study to analyze age-dependent gender differences in human liver regeneration. Validation of a regenerative advantage in women might stimulate the search for novel therapies such as the exploitation of female hormones for the improvement of surgical outcomes.

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