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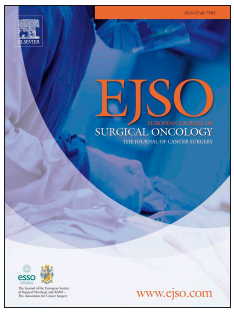

ALPPS: the argument for

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ALPPS: the argument for

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The acronym "ALPPS" was coined by de Sanibanes and Clavien in 2012 to describe surgery which involved "Associating Liver Partition and Portal vein ligation for Staged hepatectomy" following on from the initial reports over the previous two years from both Germany and Argentina.[1,2,3] The development of ALPPS appears to have been at least in part by serendipity: initially described in a single patient with perihilar cholangiocarcinoma and then tested in a series of patients with extensive colorectal liver metastases. Early reports suggested there was a very high risk or peri-operative mortality but at the same time it appeared to offer hope for patients with a high burden of disease and as a result there were both strong proponents and opponents for this innovative procedure at an early stage and much argument remains today. Whilst surgeons have often been criticised for poor scientific approaches to clinical research, we are driven by a passion to improve patient care in difficult situations. With ALPPS we have seen an excellent example of diffusion of innovation theory and we remain in limbo with an ongoing battle between relatively few early adopters and many sceptics and laggards.[4] Yet ALPPS is here to stay as a useful surgical advance and with the successive development of modifications, again through innovation, it is now clear that the early fears of excessive mortality should be laid to rest. In considering the case for ALPPS it is important to review these developments and understand properly how each has made a contribution as this is an argument that needs to be settled. This is important as there is no doubt that opinion leaders can influence adoption of new techniques.

There is no doubt that the majority of the early reports relating to ALPPS were associated with a high risk of per-operative mortality. In 2012, Schnitzbauer et al described a collaborative German experience of 25 patients with 3 early deaths (12% peri-operative

mortality) and a complication rate of 68%, but survival at 6 months was 86% for this group of apparently otherwise inoperable cases.[2] It is important to note, however, that the three patients who died accounted for 40% of all of the complications, all three had undergone neoadjuvant chemotherapy for colorectal liver metastases, and the deaths were related to biliary complications and sepsis. The major impact of this report related not only what seemed at the time to be an unusual level of risk but also more positively to the rapid future liver remnant (FLR) hypertrophy that occurred over a median of only 9 days, although the second stage was carried out over a large range of 5 to 28 days. de Sanibanes and Clavien subsequently suggested that a 7 day interval between the two stages is enough but this remains an area for debate.[1]

There are three ways that the results for ALPPS can be improved: patient selection, timing of the second stage and modification of the surgical technique. Work has been done on all of these aspects and not least in patient selection.

If we are to move forward successfully with ALPPS then patient selection will be paramount both in terms of avoiding peri-operative mortality but also for improved long term outcomes. A so called "futility risk score" has been proposed for reducing peri-operative mortality and this suggests caution for older patients and those with biliary tract cancer but more work needs to be done.[5] Data from the International ALPPS Registry suggests better outcomes with colorectal metastases cases but this is also where we have most experience with multi stage liver surgery of any type.[6] There is no doubt that in the initial experiences the rates of early tumour recurrence were too great but this is improving with time with better patient selection. It is currently not clear if there is a true advantage to ALPSS versus a more classical two stage approach but emerging data suggest that there are higher completion rates for the second stage surgery with ALPPS, although at a cost of a higher complication rate. We should not forget, however, that when two stage liver surgery was introduced there were reports of high peri-operative mortality and uncertain long term outcomes yet today this technique is widely accepted so with more careful exploration ALPPS too should earn its rightful place in hepatic surgery.

Timing for the second stage of ALPPS is a subject of ongoing discussion. The initial reports included manoeuvres including complete right liver mobilisation and enclosing the liver to be subsequently resected in a plastic bag to prevent adhesions and it was also thought that biliary drainage may be helpful. Today, most of us would agree that it is safer to carry out a less invasive first stage, not to mobilise the right liver, and to use haemostatic materials between the cut parenchymal surfaces as an easier and safer procedure. This allows more options when considering timing of the second stage, which is the operation with the greatest impact physiologically in my experience. When considering the correct timing for the second stage, ALPPS appears to engender a more rapid an improved future liver remnant volume than portal vein embolisation alone. Indeed, in Schnitzbauer's original description the median hypertrophy was 74% after an interval of only nine days, and this has been confirmed by a recent meta-analysis.[7] But, we have to question if hypertrophy as seen on a CT scan will translate to adequate post resection liver function. This is an important point as there is much remaining argument about whether volumetry or functional analysis of the FLR is more important: does hypertrophy actually mean predictable improved FLR function at an early stage or should we wait longer? Tanaka has suggested that we should be cautious as functional changes in the FLR lag behind changes in volume.[8] My own opinion is that we should indeed wait longer and I suggest that surgeons should consider that a "delayed ALPPS" approach is safer: in my experience a wait time of 14 days does not increase operative difficulty and it carries with it the benefit of easy scheduling, whilst allowing the patient some time at home between stages. We also know that successful outcomes are possible with "rescue ALPPS" for patients that have previously failed to achieve adequate FLR hypertrophy with portal vein embolisation.

With any new surgical procedure there will be inevitable alterations in technique suggested to improve outcomes. There have been recent reports of zero peri-operative mortality in series of carefully selected patients with success was partly attributed to careful preservation of the middle hepatic vein during the first stage. This more partial hepatic transaction at stage one was highlighted by Clavien's group in 2015 as partial ALPPS (or p-ALPPS) and described as a 50-80% transaction associated with a reduction in mortality from 22% down to zero so this was a significant observation.[9] Importantly, FLR hypertrophy does not appear to be compromised by this technique. Others have described this approach as a

"mini-ALPPS" and the aim has been to limit morbidity between the two stages. Most recently, the minimal invasive approach of laparoscopic ALPPS has also emerged as a way of reducing the morbidity of both stages. These are significant advances that must not be ignored. At the more radical end, "monosegment ALPPS" and "hybrid ALPPS" also deserve consideration. Schadde et al reported 12 cases of monsegment ALPPS from the international ALPPS registry, leaving a single hepatic segment FLR, with no operative mortality in 2015.[10] It is clear that careful patient selection and meticulous surgical technique was required. A further consideration is a "hybrid ALPPS" approach for cases where the portal bifurcation is involved with tumour and right portal vein ligation cannot be achieved without tumour compromise: here there are options of portal vein embolisation or portal vein division and re-anastomosis to occlude the portal supply to the liver to be removed at the second stage. The reality is that all of these techniques are useful and a surgeon undertaking ALPPs must be aware of new developments to maximise patient safety.

Finally, we must consider the place of ALPPS. There is no doubt that these complex procedures must only be undertaken by experienced surgeons in a high-volume centres, and patient selection should be by means of a multidisciplinary team effort. The management careful of these patients during the postoperative course of both surgical procedures is crucial to achieve success. With increasing experience, ALPPS will define its own place in the surgical armamentarium. Whist it is true that advances in chemotherapy mean that more major resections are undertaken less often these days, as liver surgeons we are faced with unexpected challenges and it is only through innovation that we can rise to the task in hand. ALPPS in its many forms is here to stay but I suspect there will be an increasing recognition that more careful patient selection along with a more minimal first stage (laparoscopic, partial and mini ALPPS) and a less urgent approach to the second stage (delayed ALPPS) will be rewarded by improved success.

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