European Survey on the Application of Vascular Clamping in Liver Surgery

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Abstract

Background: This study evaluated the frequency, the indications and techniques of vascular clamping during liver resection and during thermal destruction therapies, as currently used by hepatic surgeons throughout Europe. *Methods:* A web-based questionnaire was distributed among 621 physicians, including all members of the European Hepato-Pancreato-Biliary Association and the European Surgical Association. *Results:* The overall response rate was 50%. During liver resection, vascular clamping is never applied by 10%, on indication by 71%, and routinely by 19%. Routine clamping is particularly performed by high-volume and senior surgeons and appears to be associated with longer ischaemia times. Intermittent inflow occlusion is the clamping method of choice for more than 65% of surgeons and total ischaemia times are usually limited to 15–30 min. During thermal ablation, vascular clamping is never used by 57%, on indication by 37%, and routinely by 7%; it is particularly applied for large tumours and for tumours close to large vessels, and ischaemia times are shorter. *Conclusions:* Vascular clamping during liver resection is frequently used; during thermal ablation it is preserved for larger tumours or tumours in the vicinity of large vessels. Complete inflow occlusion is the most frequently used technique, with a distinct preference for intermittent clamping.

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Introduction

Surgical removal is the treatment of choice for many primary and secondary liver tumours, providing a potentially curative treatment [1–3]. During hepatectomy, intraoperative haemorrhage is common, often necessitating blood transfusion, which is associated with unfavourable short- and long-term postoperative outcome [4–6]. Therefore, approaches to control intraoperative bleeding are warranted and include vascular clamping methods. For non-resectable liver tumours thermal destruction techniques, such as radiofrequency ablation, laser-induced thermotherapy and microwave therapy, provide local tumour control and improve life expectancy [7–9]. During thermal ablation, vascular clamping is advised to reduce dissipation of the generated heat, which creates larger destruction volumes, resulting in greater tumour-free margins [10–12].

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Table 1. Response rates per country

Country[1]	Invited	Partici-pated	Response rate, %
The Netherlands	64	52	81
United Kingdom	100	41	41
Italy	70	37	53
Germany	66	34	52
France	43	18	42
Greece	38	16	42
Sweden	20	12	60
Norway	24	12	50
Switzerland	19	11	58
Belgium	15	9	60
Spain	18	9	50
Poland	14	7	50
Turkey	16	6	38
Denmark	10	5	50
Austria	13	5	38
Czech Republic	6	5	83
Overall	621	311	50

[1] Countries with 4 or less responders include Portugal (4), South Africa (4), Israel (4), Russia (4), Slovenia (3), Lithuania (3), Lebanon (2), Finland (1), Egypt (1), Ireland (1), Romania (1), Cyprus (1), Tunisia (1), Slovak Republic (1), Luxembourg (1).

The disadvantage of vascular clamping is ischaemia/reperfusion injury to the remaining liver which may contribute to postoperative liver dysfunction and morbidity [13]. In addition, we recently found that ischaemic damage resulting from prolonged vascular inflow occlusion may adversely affect oncological outcome by accelerating the outgrowth of colorectal micrometastases [14, 15]. On the background of these previously unrecognised adverse effects of vascular clamping on outcome, it is of great importance to know how often and to what extent vascular clamping methods are currently used in daily practice.

Several different clamping techniques have been described, each with its own advantages and disadvantages with respect to haemodynamic stability, the duration of the procedure, blood loss, the degree of ischaemia/reperfusion damage and tumour growth stimulation [14, 16–24]. However, the application of vascular clamping in daily practice during partial liver resection and thermal destruction therapy depends on the individual surgeon's judgement and preference. The aim of this survey was to gain insight into the frequency, the techniques and the indications for vascular clamping, as used by surgeons throughout Europe.

Materials and Methods

Invitations to participate in the survey were sent to 429 active members of the European Hepato-Pancreato-Biliary Association (EHPBA) and to 202 members of the European Surgical Association (ESA). In addition, the questionnaire was forwarded to 28 Dutch liver surgeons known from personal networks, including all members of the Dutch Liver Surgery Working Group. Participants also had the possibility to invite colleagues to participate in the survey, which occurred in 15 cases. Due to 53 overlapping memberships, a total of 621 invitations were sent across 39 countries in and around Europe. The questionnaire was available online and could be entered with a username and password that was provided by e-mail. After 4 weeks a reminder was sent to all non-responders and another 6 weeks later, a final reminder was sent by postal mail. The survey was closed on September 1, 2006.
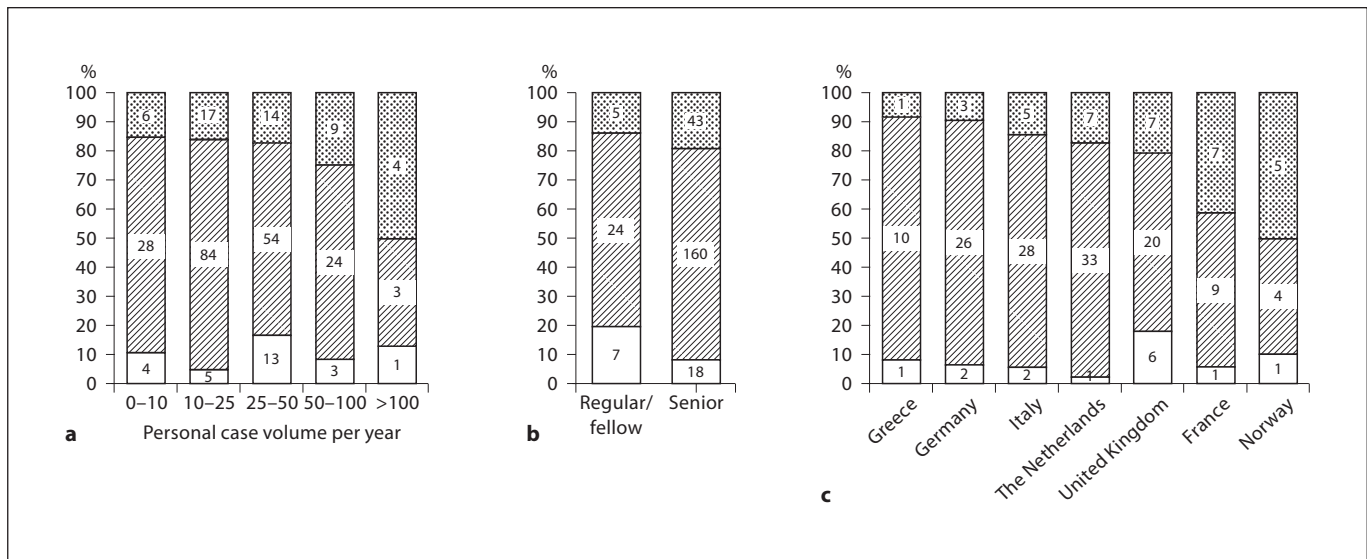
As the application of vascular clamping depends on the surgeon's individual preference, each surgeon was asked to fill out the questionnaire separately. The questionnaire consisted of four parts: (I) demographic data, (II) vascular clamping during liver resection, (III) vascular clamping during thermal ablation, and (IV) suggestions and comments. For both liver resection and thermal ablation the personal case volume per year was asked as well as the frequency, indications and contraindications for vascular clamping. Participants were asked what clamping technique was used with regard to the extent, the type and total ischaemia times. For most questions a 4-point scale 'never-sometimes-usually-always' was used. Part II also included questions on transection techniques and additional measures to control intra- and postoperative blood loss. Part III included questions on the ablative technique as well as the approach. Answers from returned questionnaires were extracted from the online database and were evaluated on a personal basis. Sub-analyses were performed according to country (including those with more than 10 responders to search for any geographical preferences), the personal case volume per year, function and type of hospital.

Statistical analysis was performed when appropriate. Pearson's χ^2 test was used for frequency analysis in 2×2 tables and the Kendal correlation for tables with ordinal variables. Mann-Whitney U and Kruskal-Wallis statistics were used for analysis of non-parametric data. A p value <0.05 was considered statistically significant.

Results

Part I. Response Rates

We received 311 responses from 31 countries, yielding an overall response rate of 50%. The geographic distribution is shown in table 1. Of all responders, 39 indicated not to actively practice hepatic surgery. Of the remaining responders, 269 completed Part II and 227 completed Part III, corresponding to specific response rates of 43 and 37% respectively.

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Fig. 1. Application of vascular clamping during liver resection according to (**a**) personal case volume per year, (**b**) function and (**c**) country (▓ = routinely; ▨ = on indication; ▢ = never).

Part II. Vascular Clamping during Liver Resection

Frequencies

Personal case volumes per year, function and type of hospital of all 269 responders practicing liver resection are shown in table 2. Vascular clamping during liver resection is never applied by 10%, on indication by 71%, and routinely by 19% of surgeons. Interestingly, routine clamping appears to be more frequently applied by surgeons with a high personal case volume per year (p = 0.033) and senior surgeons (p = 0.089) (fig. 1a, b). Based on the minimum and maximum case volumes for each individual surgeon, it can be calculated that an estimated 24% of all patients are clamped routinely each year. Furthermore, routine clamping is more common in Norway and France, whereas 18% of respondents from the United Kingdom never clamp during hepatectomy (fig. 1c). The clamping preferences of surgeons from university hospitals were similar to those from local hospitals.
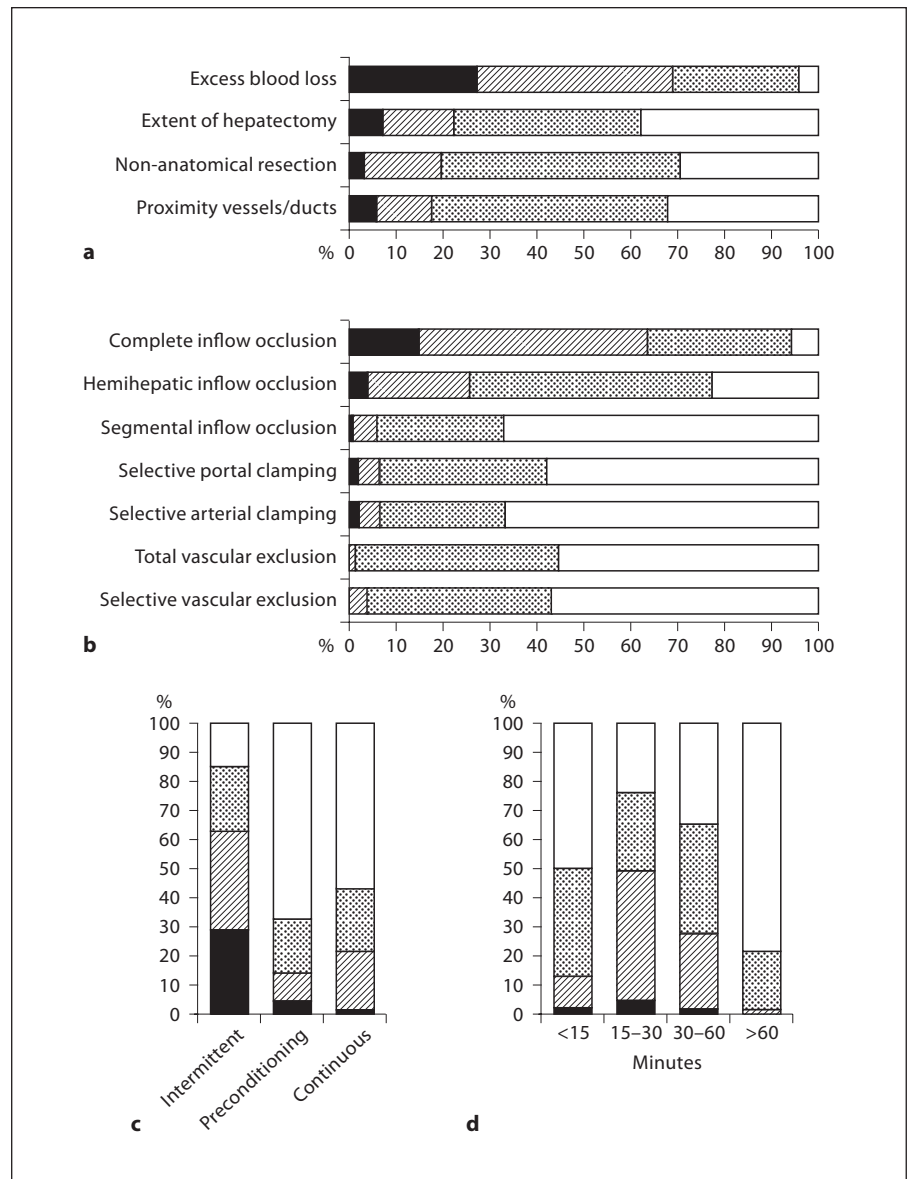
Indications and Contraindications

The prime indication for vascular clamping used by 69% of surgeons is excessive blood loss (fig. 2a). The median cut-off point for applying vascular clamping is 500 ml, but ranged from 100 to 5,000 ml. Other common indications for vascular clamping include: major hepatectomy of a median of 3 (range 1–6) segments, non-anatomical resections or proximity to large vessels or bile ducts (fig. 2a). Rare indications (3%) include central hepatectomy, segmental resection, anatomical variations, clinical trials, chemoperfusion, Jehovah's Witness, cirrhosis, very precise dissection, 'depends on localization or individual situation' and hepatic trauma.

Table 2. Personal case volumes, function and type of hospital of responders performing liver resection and local ablation techniques

|	Liver resection		Local ablation	
	n	%	n	%
Personal case volume/year				
<10	38	14	88	39
10–25	106	39	87	38
25–50	81	31	34	15
50–100	36	13	14	6
>100	8	3	4	2
Function				
Senior	220	82	184	81
Regular/fellow	36	13	31	14
Other/unknown	13	5	12	5
Type of hospital				
University hospital	214	79	178	78
Regional/local hospital	50	19	45	20
Other/unknown	5	2	4	2
Overall	269	43	227	36

Fig. 2. Indications and techniques for vascular clamping during liver resection. (**a**) Indications specified by 193 surgeons. The extent (**b**), type (**c**) and total ischaemia times (**d**) of vascular occlusion for all surgeons performing vascular clamping during liver resection, either on indication or routinely (n = 243) (■ = always; ▨ = usually; ▨ = sometimes; □ = never).

We also searched for contraindications by asking 'Would you consider applying vascular occlusion in cirrhotic, steatotic and post-chemotherapy livers?' All three circumstances appear to be relative contraindications as 72–76% of surgeons would never or only sometimes apply vascular clamping in these situations. For surgeons who apply vascular clamping on a routine basis, these situations are regarded as contraindications less frequently.

Technique (Extent, Type and Duration)
Complete inflow occlusion (i.e. the Pringle manoeuvre) is the most frequently applied method followed by hemihepatic inflow occlusion (fig. 2b). The more selective clamping techniques such as segmental inflow occlusion, selective clamping of the portal vein or hepatic artery, total vascular exclusion and selective vascular exclusion (with preservation of the caval vein) are less commonly used (fig. 2b). Interestingly, the Pringle manoeuvre is more frequently used by senior surgeons when compared to regular/fellow surgeons (63 vs. 21%, $p < 0.001$), whereas regular/fellow surgeons use hemihepatic clamping more often (79 vs. 23%, $p < 0.001$). The vascular exclusion techniques are predominantly, but not exclusively, performed by high-volume experts. Intermittent

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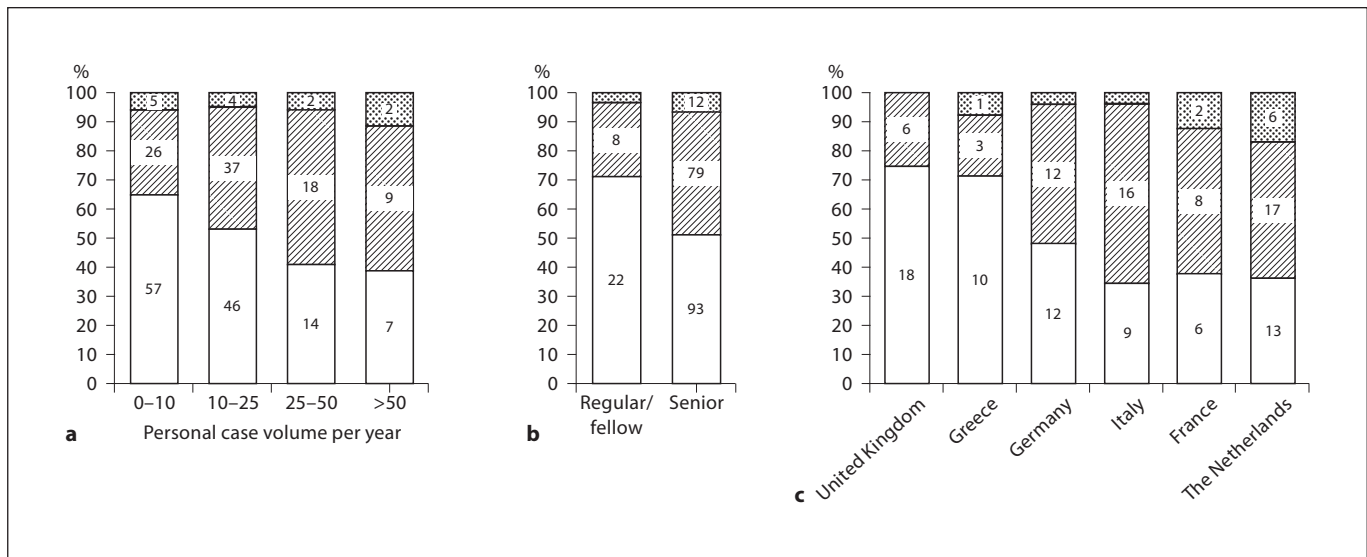
Fig. 3. Application of vascular clamping during local ablation according to (**a**) personal case volume per year, (**b**) function, and (**c**) country (▨ = routinely; ▧ = on indication; ☐ = never).

clamping is the most frequently applied method (63%) with a typical clamping strategy of 2–3 cycles of 15–20 min of ischaemia and 5–10 min of reperfusion (fig. 2c). Ischaemic preconditioning and continuous clamping are less commonly used (14 and 21%, respectively). The distinct preference for intermittent clamping was irrespective of whether clamping was performed routinely or on indication, the personal case volume per year, function, type of hospital or country.

Ischaemia times are usually limited to 15–30 min and clamping >60 min is only used scarcely (fig. 2d). This is irrespective of whether clamping is performed intermittently, with preconditioning or continuously. Ischaemia times tend to be slightly longer during routine clamping and by high-volume experts (data not shown). With ischaemia times exceeding 30 min in 40% of the patients who are clamped on a routine basis (by 24% of surgeons), it can be calculated that an estimated 10% of patients are routinely clamped for longer than half an hour by this cohort of surgeons every year.

Other Methods to Control Intraoperative Blood Loss
Of the transection devices aimed at controlling blood loss, the CUSA is most frequently used (56%; sometimes by 16%). Precoagulation devices are usually or always used by 23% and sometimes by 34%. Other transection devices, indicated by 22% of surgeons, include ultrasonic dissector, harmonic scalpel, bipolar, LigaSure, diather-

mia, staplers, finger fracture and Kelly fracture. The use of precoagulation devices correlated to the clamping preference: 15% of surgeons who prefer precoagulation never clamp during resection versus 8% of surgeons who sometimes or never use these devices (p = 0.014).

The maintenance of a low central venous pressure is a standard procedure for the majority of surgeons (always 55%; usually 32%; sometimes 7%). The application of a low central venous pressure does not correlate to the clamping preference, but is inversely related to the personal case volume per year, as it is more frequently omitted by less experienced surgeons (p < 0.010). The median accepted pressure is 5 cm H_2O (range 1–10). Additional strategies to control blood loss include: clips (71%), argon beamer (50%) and biological products, such as glues and patches (43%). Other measures (9%) involve: sutures, staplers, tissue compression, omentum and high-pressure pneumoperitoneum during laparoscopic liver resection.

Part III. Vascular Clamping during Local Ablation

Frequencies
Of the 227 responders practicing thermal destruction techniques the majority perform radiofrequency ablation (90%) through the open (44%) or percutaneous (34%) approach. Personal case volumes, function and
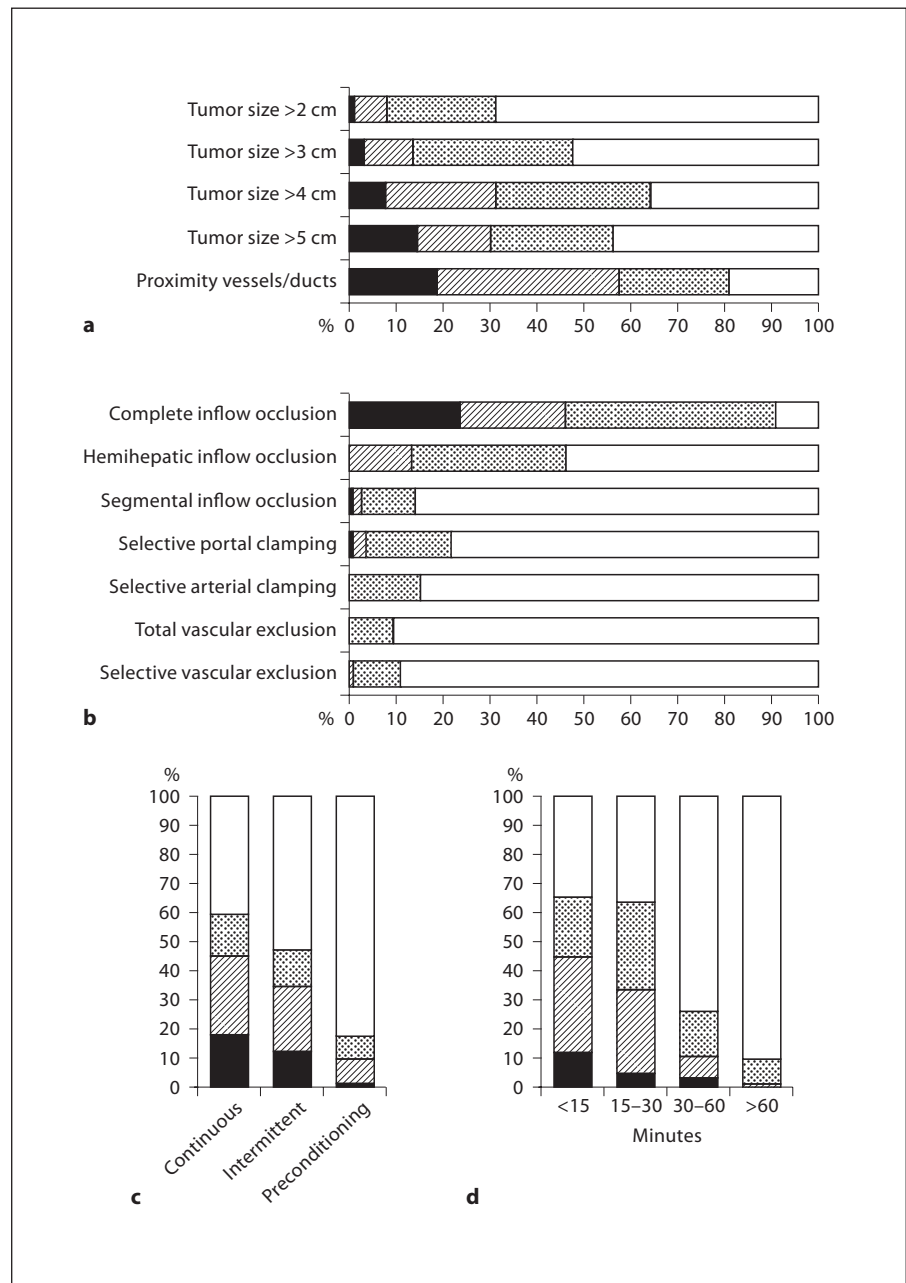
Fig. 4. Indications and techniques for vascular clamping during local ablation. (**a**) Indications specified by 89 surgeons. The extent (**b**), type (**c**) and total ischaemia times (**d**) of vascular occlusion for all surgeons performing vascular clamping during liver resection, either on indication or routinely (n = 102) (■ = always; ▨ = usually; ▨ = sometimes; □ = never).

type of hospital are shown in table 2. Vascular clamping to increase lesion size during thermal ablation is never applied by 55%, on indication by 40%, and routinely by 6% of surgeons. Clamping is more frequently omitted by low-volume surgeons (p < 0.010, fig. 3a) and regular/fellow surgeons (p = 0.040, fig. 3b). It is more routinely applied in The Netherlands and France and is most frequently omitted in the United Kingdom and Greece (fig. 3c).

Indications and Technique (Extent, Type, Duration)

Indications for vascular clamping during local ablation include increasing size and location near large vessels or bile ducts (fig. 4a). The majority of surgeons apply the Pringle manoeuvre; other methods are used scarcely (fig. 4b). In contrast to liver resection, continuous clamping is more frequently used than intermittent clamping (fig. 4c) and ischaemia times are often <15 min (fig. 4d). Surgeons who clamp on a routine basis use intermittent

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clamping (39%) more often than continuous clamping (8%), which is associated with longer ischaemia times (15–30 min in 46%). The preferences for the clamping technique appear not to be related to the personal case volume, function or the type of hospital.

Part IV. Additional Commentaries

Additional remarks were made by several surgeons, which partly overlapped the results as described above. Most importantly, many surgeons underscore that there is no standard policy for clamping, but that the choice for the different techniques is highly individualized. Several surgeons only use inflow and/or outflow occlusion for atypical, difficult or central hepatectomies or for tumours involving the porta hepatis. It was also indicated by several surgeons that selective clamping techniques are preferred for diseased livers. Moreover, continuous clamping seems to be particularly used for selective clamping methods, whereas, during complete inflow occlusion and vascular exclusion, intermittent clamping is preferred. Another important aspect of bloodless liver surgery indicated is the ligation of afferent and efferent vessels of the involved lobes prior to splitting of the parenchyma. Finally, the use of intraoperative ultrasound and good cooperation with expert anaesthetists is mandatory for performing bloodless hepatic surgery.

Discussion

The findings of this survey provide a comprehensive insight into the frequencies, indications and techniques of vascular clamping as currently used by hepatic surgeons throughout Europe, both during hepatic resection and thermal destruction techniques. With an overall response rate of 50%, including the majority of surgeons associated to the EHPBA and ESA, the results are likely to be representative for the global practice of particularly experienced hepatic surgeons.

The results primarily demonstrate that vascular clamping is commonly applied during liver resection: approximately 1 out of 5 surgeons clamp on a routine basis. This is consistent with a Japanese survey on control of intraoperative bleeding showing that 25% of surgeons routinely clamp during resection [25]. Interestingly, routine clamping is most frequently applied by surgeons with a high personal case volume and by senior surgeons, which may reflect the more complex operations they per-

form. This is substantiated by the more frequent use of total vascular exclusion techniques and longer total ischaemia times by high-volume experts. Nonetheless, based on the notion that senior surgeons use a standard Pringle manoeuvre more often, whereas regular/fellow surgeons use more selective clamping techniques, it may also be challenged that senior surgeons apply their vascular clamping methods more habitually.

Although the decision process for the appropriate clamping technique depends on the combination of several individual patient characteristics and technical aspects, blood loss remains the prime indication for temporary blood flow occlusion. Remarkably, the maximally allowed amount of blood loss varied greatly among surgeons, representing variance in risk assessment. Paradoxically, both excessive blood loss and vascular clamping have been associated with unfavourable short- and long-term postoperative outcome [4–6, 13–15], but it is currently unknown to what extent blood loss may be accepted without the adverse effects of vascular clamping and vice versa. This warrants further evaluation to support a universal recommendation. Whereas for some responders the cirrhotic liver is an indication because of a higher bleeding tendency, others find it a relative contraindication due to concerns about decreased tolerance to ischaemia [26, 27]. Steatotic and post-chemotherapy livers also have increased susceptibility to ischaemic damage [18, 20, 28, 29], which is reflected by a general reluctance to apply clamping in such livers. The clamping method of choice in post-chemotherapy livers is not yet well defined, which is becoming even more relevant, as pathophysiologic changes in the liver after chemotherapy are described in 19–92% of patients [29–33].

Among a variety of vascular clamping techniques, the Pringle manoeuvre is the most popular form of vascular occlusion, followed by hemihepatic clamping. Selective clamping techniques and the total vascular exclusion techniques are rarely used on a routine basis, but about one third of surgeons apply these techniques when necessary or appropriate. Good knowledge of all the benefits and drawbacks of the different techniques available is a prerequisite for appropriate individualized application of vascular clamping [21–23, 34].

The attention in recent years for ischaemia/reperfusion injury resulting from prolonged continuous clamping has clearly led to a distinct preference for techniques that protect the liver from ischaemic damage, such as intermittent clamping or ischaemic preconditioning [18, 20, 35]. Overall, ischaemia times are usually within 30 min, nonetheless, we calculated that 1 out of 10 patients

are routinely clamped for longer than half an hour. The normal human liver seems to tolerate continuous normothermic ischaemia of up to 60 min and intermittent ischaemia of up to 120 min relatively well [36, 37]. Nonetheless, although prolonged vascular clamping may be performed without any severe postoperative morbidity or mortality, clamping periods of >20–30 min may induce severe long-term adverse effects by accelerating the outgrowth of residual disease [14, 15].

Recent reports have indicated that major liver resection can be safely performed without vascular clamping [38, 39], and 10% of responders from this survey confirm this idea. The tendency to withhold from clamping may partly be the result of advances in parenchymal transection [40, 41], including the use of precoagulation devices [42, 43]. In fact, the frequent use of precoagulation correlated with less frequent use of clamping. The maintenance of a low central venous pressure did not correlate with the application of vascular clamping, but owing to the proven reduction in blood loss resulting from this procedure [44–48], it has become a standard procedure for the vast majority of surgeons. We found a considerable variation in the maximally allowed central venous pressure, which deserves further attention. During laparoscopic hepatectomy, vascular occlusion may also be omitted more frequently [49], but this was not questioned in this survey. In general, in light of the previously unrecognised putative adverse effects of vascular clamping on oncological outcome, vascular clamping may be omitted more frequently in the future.

Given the evidence that vascular clamping during thermal destruction therapy is an essential part of the procedure for obtaining a safer margin around the ablated tumour [50], particularly in larger tumours and tumours located near large vessels [50, 51], it is surprising that more than half of all responders never clamp during ablation. This may partly be explained by the fact that some surgeons do not treat patients with tumours >4 cm. On the contrary, these numbers may actually represent a relative overestimation, because vascular clamping is seldom used during the percutaneous approach and nowadays many patients are treated percutaneously by interventional radiologists, who were not included in this survey. These findings emphasize the need for uniform guidelines for vascular clamping during ablative therapies. During local ablation, the Pringle manoeuvre is chosen by the majority of surgeons. Portal clamping, which is applied by 4% of surgeons, may be advantageous in thermal destruction techniques, as it provides an increase in lesion size, but minimizes ischaemic damage

[10, 24]. By those who clamp routinely during local ablation, intermittent clamping is favoured, corresponding to ischaemia times of 15–30 min, whereas for the majority of surgeons who clamp on indication, a shorter continuous Pringle manoeuvre seems to be preferable.

In conclusion, the major findings of this survey demonstrate that vascular clamping during liver resection is commonly applied, whereas during local ablation techniques it is preserved for larger tumours or tumours in the vicinity of large vessels. Among a variety of vascular clamping techniques, the Pringle manoeuvre is the most popular technique, with a distinct preference for intermittent clamping. The finding that 1 out of 10 patients is clamped routinely for >30 min underscores the need for further clinical investigation of protective strategies against the adverse effects of prolonged vascular clamping on long-term outcome. Variations in the maximally accepted amount of blood loss and central venous pressure demonstrate the importance of uniform recommendations for these issues. Finally, universal guidelines for vascular clamping during local ablation are needed.

Acknowledgements

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Invited Commentary

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It has been very interesting to read the article of van der Bilt et al. on methods to control hepatic blood flow during both thermal ablation techniques and liver resection that are currently used in Europe. They report on data of a survey on the frequency, indication and techniques of vascular clamping during liver resection. Their analysis clearly shows that there is no common strategy for applying vascular clamping during liver resection, nor a particular technique of clamping or method used for liver transection. After subgroup analysis the authors state that the Pringle maneuver with intermittent clamping is the most frequently applied method.

Usually, response rates of up to 30% can be expected with questionnaires used for a survey; however, the authors managed to obtain a feedback from 50% of all participants. The authors have to be congratulated for this success and the scientific community should further support similar studies. Assuming that data shown here are based on the routine practice of representative European surgeons and centers, it can be concluded that vascular clamping, i.e. complete inflow occlusion (Pringle maneuver), is still quite frequently used. This result is surprising if one analyzes the background, history and recent developments in liver surgery.

The detrimental impact of excessive hemorrhage and blood transfusion of patients undergoing liver resection is well documented. Back in the late 1970s the operative mortality was 13% and more than 20% for major resections, with 20% of deaths resulting from intraoperative bleeding [1]. Further, excessive blood loss is associated with increased perioperative morbidity and, in case of colorectal metastases, a shorter disease-free interval [2, 3].

Almost 100 years ago a lecturer on surgery at Queen Margaret College and surgeon to the Glasgow Royal Infirmary named J. Hogarth Pringle published his first experiences with a method to control the hepatic inflow, later called the 'Pringle maneuver'. Unfortunately, all of his reported patients died shortly after or even during surgery [4]. Nevertheless, his method, the occlusion of the hepatic inflow, and total vascular occlusion introduced by Bismuth et al. [5] and Huguet et al. [6], turned out to be a crucial tool for the pioneers of liver surgery to successfully perform liver resections almost 20 years ago.

Today the use of vascular control of the liver indeed still seems to highly depend on the surgeon's individual preference without evidence-based scientific background supported by randomized controlled trials as mentioned by van der Bilt et al. It even appears to be that vascular

clamping during liver surgery still is a dogma for senior surgeons. According to their survey, the Pringle maneuver was used by senior surgeons in about 40% more cases than it was applied by regular/fellow surgeons. Since evidence-based medicine works against dogma, one should realize that the control of the hepatic blood flow may not be as important today as it was several years ago.

Today, subtle nuances in surgical technique can make a substantial difference in patient outcome. Various surgical techniques, instruments and an optimized intraoperative anesthesiological support of the patient have been developed for safe tissue-preserving dissection of the liver parenchyma to prevent complications with operative morbidity and mortality rates typically being less than 30 and 5%, respectively, in high-volume centers [7, 8]. In parallel, a rapidly declining transfusion rate has been documented during the last years [9]. Our most recent clinical data strongly support the hypothesis that blood loss can be minimized with selected surgical techniques for parenchymal dissection even without the use of vascular clamping [8].

The concept of liver resection omitting vascular clamping is further supported by most recent clinical data. They clearly indicate that non-selective intraoperative vascular control, i.e. total vascular occlusion and Pringle maneuver, is associated with unpredictable hemodynamic instability, post-reperfusion hypotension, increased catecholamine support, increased interleukin release correlating with postoperative injury to the remnant liver, delayed hepatocyte regeneration, and increased postoperative complications with longer hospital stay [10–13]. Further, especially in both steatotic and fibrotic livers, failure of the liver remnant together with an increased mortality, ascites and encephalopathy can be observed more often after the Pringle maneuver [14]. Besides these immediate effects of vascular clamping in liver surgery, van der Bilt et al. discuss putative adverse effects on oncological outcome.

In summary, both excessive blood loss and vascular clamping are associated with unfavorable short- and long-term outcome after liver resection. Based on the only two randomized controlled clinical trials with level 1 evidence that are available today, there is no difference in any of the relevant clinical parameters between patients who underwent liver resection with or without hepatic inflow control [15, 16]. However, since it remains unclear to what extent blood loss is acceptable without the adverse effects of vascular clamping and vice versa, clinical trials are warranted to further optimize patients' benefit of liver surgery.

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Invited Commentary

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The paper by van der Bilt et al. presents the results of a European survey on current practices regarding vascular clamping during both liver resectional surgery and liver tumour ablation. The inspiration for the survey was provided by their previous observation of stimulation of micrometastatic tumour growth by ischaemia/reperfusion in a murine model [1]. A further interesting observation was that intermittent clamping did *not* stimulate outgrowth, the effect was limited to an ischaemic preconditioning protocol.

The results of the survey indicated that clamping practices are variable but clamping is applied by about 90% of surgeons during hepatectomy, and routinely by 19%. Clamping is more likely with high-volume and senior surgeons and 65% use intermittent clamping. Generally, short clamping periods are desired with most preferring no more than 30 min.

Putting aside for the moment the putative effect of ischaemia/reperfusion and oncological outcome, the current evidence regarding pedicle clamping or no clamping could best be summarized as one of clinical equivalence. The first randomized trial of clamping vs. no clamping [2] demonstrated benefits for clamping particularly with respect to blood loss. The second and more recent randomized study [3] did not demonstrate any difference. Further laboratory and clinical studies have demonstrated the safety of pedicle clamping and the superiority of intermittent clamping and ischaemic preconditioning over continuous clamping [4–7]. In older subjects, and those with diseased parenchyma, there is emerging evidence, both laboratory and clinical, that intermittent clamping is the preferred technique [5, 6, 8, 9].

From the perspective of the hepatic surgeon, clamping is applied to reduce blood loss and present a clear field for surgery. While evidence has been acquired to suggest an inferior outcome in patients requiring transfusion [10], a positive benefit on outcome with respect to survival or a decrease in positive resection margins secondary to pedicle clamping has not been directly demonstrated.

Considering the above evidence it seems perfectly reasonable that hepatic surgeons have adopted their current practice of clamping according to individual preference and circumstance. It is perhaps a little surprising that intermittent clamping is not used more frequently than 65%, but this could be accounted for by the relatively short periods of clamping reported.

No published clinical studies (at the time of writing this commentary) have addressed the relationship between pedicle clamping and long-term outcome, particularly with reference to survival or frequency and site of tumour recurrence. Our own clinical study did not reveal any difference in overall or disease-free survival relative to clamping [11]. We await the publication of clinical evidence from the authors of the current study.

The relationship between pedicle clamping and the outgrowth of micrometatstases, and by inference long-term survival, remains speculative. Both selective portal clamping and intermittent clamping offer protection against this phenomenon in the murine model [1, 12]. The observation is nonetheless important and careful work is required in both the laboratory and clinical setting to confirm or otherwise refute its validity.

At our current state of knowledge it seems reasonable to recommend that exercising individual preference for careful pedicle clamping is still appropriate, but that intermittent clamping should be used in preference to other clamping protocols, particularly in older patients, those with abnormal parenchyma or if more prolonged clamping is to be applied. Whether or not this recommendation needs to be modified because of an effect of pedicle clamping on tumour-specific survival will no doubt be the subject of significant future endeavour.

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