Introduction
For years, the issue of centralization in liver surgery in specialist 'high-volume' hospitals has been prominent in the debate on improving quality in healthcare. It is well established that high volume, in general, means better outcome, and many studies have shown lower mortality and higher survival rates in high-volume versus low-volume centers (1-6). Indeed, in high-volume centers 90-day mortality rate is approximately 3%, with the morbidity rate around 30% (7-10). The factors involved seem to be many: better knowledge of the anatomy, more accurate selection of patients, refinements of surgical perioperative medicine techniques, as well as optimization of the management of postoperative complications (11-15).

The present review involves all available literature on the relationship between hospital or surgeon volume and postoperative mortality and survival in liver surgery suggesting some guidelines for management and creation of centralized departments.

Review of the literature
Table 1 details review of the literature regarding the relationship between outcome and volume in hepatobiliary surgery. Considering the rapid evolution of liver surgery, we have included articles published in the last 20 years in English. Moreover, we have included only those articles that have declassified hepatobiliary surgery from pancreatic surgery, which are usually considered together (16-45). As detailed, almost all the included articles supported a positive relationship between hospital volume and outcome indicating the validity of the union of high-volume and high-quality. In particular, in 2003, Dimick et al. (20) analyzed more than 2,000 hepatectomies performed in North America and found that those institutions that performed more than 20 resections per year had significantly lower mortality. Although the resulting cut off of 20 resections per year seems too inclusive, objectively the differences were substantial. However, in both groups the mean values outranged the benchmarks even of that period (6.3% vs. 15.5%). In 2009 a systematic review and in 2012 a meta-analysis confirmed a reduced mortality risk after liver surgery in high-volume centers (46,47). Few of these articles, investigated how this relationship was mainly based on hospital or organization factors rather than on surgeon factors. In general, the positive relationship was evident both for the hospital and surgeon volumes. Even if this is reasonable, there...
are confounding factors that are difficult to separate. In this sense, it is important to note that it is difficult to distinguish when high quality care in complex surgery is a consequence of reaching the plateau of a learning curve or when it is the consequence of a standard volume that is a minimum number of procedures per year. Besides, it is important to note that good outcomes in hepatobiliary surgery are also related to the quality of other hospital services, such as the anesthesiology service and the intensive care unit, which similarly to the surgeons have to reach the plateau of their learning curves. In this sense, further studies should be conducted to better characterize these two phenomena (i.e., learning curve versus minimum standard volume).

Nathan H et al. (26) reported that the surgeon volume was not associated with in-hospital mortality, while Chang CM et al. (45) reported the combined effects of hospital and surgeon volume strongly influenced short-term survival after hepatic resection. In this latter study, the prognosis was adjusted for several different factors such as indication for surgery, quality of the underlying chronic liver disease, and socio-economic status that were found to be important to be recorded and analyzed to strengthen the relationship between perioperative outcome and surgeon and/or hospital volume. Besides, Chang CM et al. (45) figured out that the combination of high-volume surgeons in high-volume hospitals was associated with higher quality results, while the combination of high-volume surgeons in low-volume hospitals was not. Notably, in this study high-volume hospitals were those institutions performing more than 245 cases per year, while high-volume surgeons were those surgeons performing more than 59 cases per year. Notwithstanding these published studies, the definition of "high-volume center" remains to be elucidated. There is not an established cut-off of liver resections per year to perform (48).

Centralization of hepatobiliary surgery

The goal of centralization of hepatobiliary surgery is to provide optimal care of patients affected by hepatobiliary diseases within a given geographical area. This centralization passes through a complex process of assessment, development of dedicated policies, ongoing assurance and support from national government agencies, which should have the competence and authority to promote high quality care, good use of technical and technological tools, good allocation of human resources, and at the same time monitor, minimize and control the probability of unfortunate events. This process should be provided along a space-

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Table 1. Review of the literature on the relationship between outcome and volume in hepatobiliary surgery

<table>
<thead>
<tr>
<th>Author (Ref.)</th>
<th>Year</th>
<th>Patients</th>
<th>Importance of hospital volume</th>
<th>Importance of surgeon volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Begg CB, et al. (16)</td>
<td>1998</td>
<td>801</td>
<td>+</td>
<td>n/a</td>
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<tr>
<td>Choti MA, et al. (17)</td>
<td>1998</td>
<td>606</td>
<td>+</td>
<td>n/a</td>
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<tr>
<td>Glasgow RE, et al. (18)</td>
<td>1999</td>
<td>507</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Gordon TA, et al. (19)</td>
<td>1999</td>
<td>293</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Dimick JB, et al. (20)</td>
<td>2003</td>
<td>2,097</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Imamura H, et al. (21)</td>
<td>2003</td>
<td>1,056</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Fong Y, et al. (22)</td>
<td>2005</td>
<td>3,734</td>
<td>+</td>
<td>n/a</td>
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<tr>
<td>Hollenbeck BK, et al. (23)</td>
<td>2007</td>
<td>3,630</td>
<td>+</td>
<td>n/a</td>
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<tr>
<td>Epstein RW, et al. (24)</td>
<td>2008</td>
<td>2,949</td>
<td>-</td>
<td>+</td>
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<tr>
<td>McKay A, et al. (25)</td>
<td>2008</td>
<td>1,107</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Nathan H, et al. (26)</td>
<td>2009</td>
<td>6,871</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Stella M. (27)</td>
<td>2009</td>
<td>n/a</td>
<td>-</td>
<td>n/a</td>
</tr>
<tr>
<td>Chamberlain RS, et al. (28)</td>
<td>2011</td>
<td>84</td>
<td>-</td>
<td>+</td>
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<tr>
<td>Giulante F, et al. (29)</td>
<td>2012</td>
<td>588</td>
<td>+</td>
<td>n/a</td>
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<tr>
<td>Yasunaga H, et al. (30)</td>
<td>2012</td>
<td>18,046</td>
<td>+</td>
<td>n/a</td>
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<tr>
<td>Viganò L, et al. (31)</td>
<td>2013</td>
<td>106</td>
<td>+</td>
<td>n/a</td>
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<tr>
<td>Goetze TO, et al. (32)</td>
<td>2014</td>
<td>487</td>
<td>+</td>
<td>n/a</td>
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<tr>
<td>Ravaiol M, et al. (33)</td>
<td>2014</td>
<td>621</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Schneider EB, et al. (34)</td>
<td>2014</td>
<td>3,695</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Buettner S, et al. (35)</td>
<td>2014</td>
<td>9,874</td>
<td>+</td>
<td>n/a</td>
</tr>
<tr>
<td>Aldrighetti L., et al.” (35)</td>
<td>2015</td>
<td>1,497</td>
<td>+</td>
<td>n/a</td>
</tr>
<tr>
<td>Ejaz A, et al. (36)</td>
<td>2015</td>
<td>9,466</td>
<td>n/a</td>
<td>+</td>
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<tr>
<td>Buettner S, et al. (37)</td>
<td>2016</td>
<td>5,075</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Gani F, et al. (38)</td>
<td>2016</td>
<td>27,813</td>
<td>+</td>
<td>n/a</td>
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<tr>
<td>Botea F, et al. (39)</td>
<td>2017</td>
<td>3,916</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Chapman BC, et al. (40)</td>
<td>2017</td>
<td>12,757</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Idees JI, et al. (41)</td>
<td>2018</td>
<td>96,107</td>
<td>+</td>
<td>n/a</td>
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<tr>
<td>Bouras AF, et al.”’’ (42)</td>
<td>2019</td>
<td>46</td>
<td>-</td>
<td>n/a</td>
</tr>
<tr>
<td>Chen Q, et al. (43)</td>
<td>2019</td>
<td>4,902</td>
<td>+</td>
<td>n/a</td>
</tr>
<tr>
<td>Filmann N, et al. (44)</td>
<td>2019</td>
<td>110,332</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Chang CM, et al. (45)</td>
<td>2019</td>
<td>13,159</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

*Focus on gallbladder cancer; **Learning curve not hospital volume; ***Focus on laparoscopic liver surgery.
time continuum that should warrant quality in all phases of the care of patients affected by hepatobiliary diseases.

These critical issues are very important in particular in liver surgery for several reasons. First, the definition of resectability is not standardized and wide variability is, in fact, observed among expert surgeons (49). Second, the complexity of liver surgery is difficult to be classified because several different types of resections requiring an extremely wide range of expertise can be performed. A standard distinction between major and minor hepatectomies is inadequate in the current era of modern liver surgery (50). Indeed, there are different technical solutions allowing parenchymal-sparing hepatectomies, much more complex than standard major hepatectomies, that remain in the shadow of the definition of minor hepatectomy. Yet, high quality centers should not be considered those centers performing a high proportion of major hepatectomies. In this sense, a new classification for minor hepatectomy that might help in better reporting minor but complex resections has been recently proposed (51). Third, post-operative morbidity and mortality rates have a limited validity to assess quality. Centers selecting only patients operable by performing small limited resections may have lower morbidity rates in comparison with centers routinely selecting patients operable by performing complex resections. Fourth, realistic cutoffs of mortality and morbidity rates after hepatectomy as a benchmark of quality should be defined to avoid the risk of denying the chance of care to those patients with higher complexity due to tumoral presentation or advanced age or because of severe comorbidities. Apart from the specificity of their indications for surgery, which requires being addressed by the local multidisciplinary teams (MDT), risk-adjusted metrics to compare outcomes among institutions are mandatory. Otherwise the risk of unfair comparisons will remain. In this sense, a benchmarking process has been started by merging the comprehensive complications risk (CCI) (52), liver failure occurrence, and morbidity and mortality classified according to the Clavien-Dindo classification (53). Last but not least, as recently pointed out by Aloia et al. (54) there are some downsides to the strategy of aiming at zero mortality rates after surgery such as the performance of innovative operations, which at least at the beginning are not compatible with perfection that might be strongly limited in the context of no-mortality. Therefore, the centralization process in hepatobiliary surgery should pass through the development and adoption of a new and modern common language for indications, resectability, terminology of resection, and good quality indicators.

**Minimum hospital requirements in hepatobiliary surgery**

To date, there are no specific published criteria that a given hospital should have to perform hepatobiliary surgery. Most of the authors that have focused on this topic have reported their personal experiences, which anyway should be taken into consideration at least in the meantime of the reading out of some new studies with data. In 2016 a position paper published on behalf of the Italian Society of Surgery had the merit to feed up the debate and set some standards of reference (55). In Italy the current law about hospital standards is detailed by rule n. 70/2015, which divides hospitals into three levels (i.e. basic, I, and II levels). Accordingly, hepatobiliary surgery should be performed at least in level I hospitals or even better in level II hospitals, and the surgical team should be dedicated only to hepatobiliary and/or hepatobiliary and pancreatic procedures. This dedication should warrant a high-quality standard.

Moreover, those high-quality hospitals, in which hepatobiliary surgery might be performed, should have the following departments: i) Department of Medical Oncology; ii) Department of Diagnostic Radiology, which should include some interventional radiologists dedicated to hepatobiliary diseases; iii) Department of Hepatology and/or of Internal Medicine with some internists dedicated to hepatobiliary diseases; iv) Department of Digestive Endoscopy; v) Intensive Care Unit; vi) Department of Pathology; vii) Department of Nuclear Medicine; and viii) Department of Radiation Oncology.

Even stating that the above-mentioned departments should be present in any high-quality hospital certified for hepatobiliary surgery, there might be a case of a given hospital that does not have some of the previous departments. In such a case, strong operative networks between that hospital and another institution should be activated to cover any deficiency. Similarly, in such a case of a given department of hepatobiliary surgery that does not provide liver transplantation another referral center in the same geographical area should be in the network to give consultation for liver transplantation. It should not be any more allowable that a patient with complex hepatobiliary disease hospitalized in a given hospital without the titles of performing diagnosis and/or therapy for that specific disease do not provide the required network of care in the same geographical area.

**Multidisciplinary team**

Nowadays, it is mandatory to have MDT dedicated to patients affected by hepatobiliary diseases. MDT meetings provide the right global assessment of the patient both for diagnosis as well as for therapy. Any MDT meeting should include at least one member of the previous listed hospital departments with the aim to cover all the inherent aspects. Only physicians dedicated to liver diseases should take part to the MDT meeting, which should be scheduled based on
the case-load but in general once per week. A written report of the MDT should be provided for each patient with the signature of all those members that have contributed to the discussion. It is important to note that the correct functioning of the MDT meeting relies on the proper union between the scientific evidence and the local experience in the diagnosis and cure of a given hepatobiliary disease. A MDT well balanced among specialties represented, and authoritative in all its specialists, provides better patient management resulting in better short- and long-term outcomes (31,59).

Hospital volume versus surgeon volume

Ideally, hospital volume and surgeon volume should match while in the real world this is not always warranted. In hepatobiliary surgery, the relative importance of hospital versus surgeon volume is very important because both short- and long-term outcomes are dependent on hospital factors, such as the presence of intensive care unit, and surgeon factors, such as the operative technique. Nathan H et al. (26) showed that the protective effect of hospital hepatic resection volume persisted after case-mix adjustment for competing risk factors, while that was not the case considering the surgeon hepatic resection volume. Indeed, high- and low-volume surgeons had comparable in-hospital mortality rates after hepatectomy (26). There are also other factors inherent in the hospital organization which were not considered and may have biased Nathan et al. conclusions: i.e. an active MDT meeting discussing each patient as above stated, which was not considered by them and by many other authors as well.

Learning curve or standard volume?

Center volume, surgeon volume, and surgeon experience all appear to impact success rates in liver surgery. A better understanding of how these factors interact to influence outcomes could help to develop specific healthcare strategies for the improvement of the quality of care in patients with hepatobiliary diseases. As said before, it is difficult to distinguish if good outcomes in hepatobiliary surgery are more dependent on the learning curve or to a minimum standard volume. A possible strategy to overcome this infertile dualism might be the introduction of certification for hepatobiliary surgeons. Far from the idea of more bureaucracy, this strategy might include analysis of the training with emphasis on the schools of surgery, and mentors that a given surgeon might have trained under during his or her career to be entitled in performing complex hepatobiliary surgery. As recently pointed out by some authors, this was found to be a good strategy in the field of pancreatic surgery and might work also in other fields of surgery (31,59). Besides, it might be the way to reinforce the importance of schools of surgery, which are those named to train young surgeons.

Toward certified hepatobiliary surgeons

A strategy to overcome the difficulty in decoding the dualism hospital volume – surgeon volume might be the introduction of certification provided by a national board of specialists. This board should be an independent, non-profit organization founded for the purpose of certifying surgeons who have met a defined standard of education, training and knowledge. Moreover, this board might work in defining the minimum standard of care in hepatobiliary surgery on an individual basis and might analyze the applicant’s training and operative experience as well as his/her professionalism and ethics. Upon successful completion of these analyses, the surgeon might become certified in hepatobiliary surgery. This certification might serve as a prerequisite of good practice in hepatobiliary surgery, which together with the above reported minimum hospital requirements in hepatobiliary surgery, both as a single institution or as an established network between different institutions, might be warranted for high-quality care – independently by a number of procedures. Notably once certified, the hepatobiliary surgeon should undergo a process of maintenance of certification (every 5-10 years) with the aim of demonstrating ongoing professionalism and commitment to continuing medical education in the field of hepatobiliary surgery.

Conclusions

In conclusion, volume and outcome data in hepatobiliary surgery are intrinsically associated with some limitations. The published studies are mostly observational, and retrospective. Besides, the centralization process requires preparatory and preliminary agreements among experts about the development and adoption of new and modern common language for indications, resectability, terminology of resection, and good quality indicators. Without these agreements, hospital as well as surgeon volume act as proxy measures for technical and nontechnical skills. However, such a centralization process remains very important to offer better care for patients suffering from complex hepatobiliary disease.

References

3. Gordon TA, Burleyson GP, Tielsch JM, Cameron JL. The


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