specific missing data points ranged from 0.0% (sex) to 26.5% (location of incident). Across the 20 variables, 70.3% of firearm injuries had missing data compared with 56.1% of motor vehicle injuries ($P < 0.001$). Rates of missing data for patient factors, vital signs, and other clinical data were all worse in the firearm injury patients, within each category of variables all, and for all variables ($P < 0.001$) except sex ($P = 0.45$). The largest disparity in missing data was for the clinical data category, with 44.8% of firearm injury patients missing at least 1 data point compared with 26.0% for motor vehicle injuries. Specifically, the location of incident (26.5% vs 2.8%) and hospital complications (10.1% vs 6.3%) was more commonly missing for firearm versus motor vehicle injuries (both $P < 0.001$). Rates of missing data did not improve over time in patients with firearm injuries (from 70.9% $\geq$1 missing value in 2011 to 69.1% in 2014; $R = 0.0136$, P for trend <0.001).

Resnick et al utilized data from the CDC and concluded that surgeons should advocate for the establishment of comprehensive firearm injury databases,[1] like the NTDB. However, our data suggest there remains a clinically and statistically significant disparity in regards to the completeness of data in patients with firearm injuries compared with patients involved in motor vehicle trauma. These reasons for missing data points are myriad and conjecture, but likely related to a lack of patient willingness to share information for fear potential legal sequelae, the severity of their injuries, and downstream effects of laws that limit our ability to discuss firearm safety, thereby inhibiting our patient–surgeon relationship.[7] Although multiple statistical techniques exist to account for missing data, each have limitations.[5] Therefore, it is in the best interest of our current and future patients to obtain complete registry information. Without federal policy changes, however, we fear that missing data will continue to inhibit high-quality research in firearm injuries.

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Which Is the True Role of Bridging Therapies for HCC Patients Waiting for Liver Transplantation?

To the Editor:

We read with great interest the study published by Agopian et al[1] which focused on the role of loco-regional treatments (LRTs) in patients with hepatocellular cancer (HCC) waiting for liver transplantation (LT). We analyzed this paper from the point of view of main endpoints, and also ethical principles that currently dominate the allocation of liver grafts: utility (ie, post-LT outcome and recurrence), urgency (ie, pre-LT outcome), and transplant benefit (this means the difference between post-LT and pre-LT outcomes).[2]

The study by Agopian et al clearly focus on the utility endpoint (ie, risk of post-LT HCC recurrence); some of the reported results and conclusions could, however, lead to unavoidable implications on the liver allocation principles.

From the utility point of view, the main results of the study are in line with those recently reported in 2 European patient cohorts leading to the proposal of the TRAIN score.[3] Analyzing a large series of 3601 merely Milan Criteria (MC)-IN HCC cases, Agopian et al showed that poor response to LRT, pre-LT alpha-fetoprotein (AFP), and high neutrophil-to-lymphocyte ratio values were all significant risk factors for post-LT recurrence. We therefore agree with Agopian et al when stating that a static HCC model for end-stage liver disease (MELD) allocation policy taking into account only tumor size and number of fails to identify the variable risks of tumor progression, waitlist dropout, post-transplant recurrence, and survival.[1,4]

In contrast, we question the reported results in relation to the detrimental role of bridging LRT versus no treatment. In fact, this is the first and "only" study to show that LRT itself may independently predict inferior outcomes in the subset of patients unable to achieve a complete pathological response. We feel this result is not statistically solid due to a number of reasons: the degree of statistical significance is low ($P = 0.0444$); the interactions between variables in the multivariable model are not evaluated; and, finally, a multivariable analysis alone does not guarantee to eliminate the retrospective selection bias between patients with and without LRT. The last point is the most important one from a statistical point of view. Indeed, a multivariable survival analysis adjusted by inverse probability weight (obtained by propensity score calculation) would be the best methodology to evaluate the true impact of LRT on post-LT survival outcome.[5]

Even more important is the fact that the authors suggest in their main conclusion that the results of this study can be utilized to prioritize potential HCC liver recipients. The reader could interpret this study as a strong suggestion to give a high priority for transplantation to those HCC patients displaying a complete response (CR) after LRT during the waiting list period. This statement gives raise to the critical question if it is ethically acceptable to transplant patients presenting with a compensated cirrhosis in the absence of a viable (because of a CR) HCC. In this multicentre US study, about 20% of liver grafts were allocated to this particular category of patients. When looking at these patients in terms of urgency, it must be stressed that excellent survivals can be obtained not transplanting these patients, but treating them only with LRT. The liver allocation process could by doing so be optimized because allowing these "saved or spared" grafts to be implanted in patients presenting more advanced tumors or in non-HCC patients presenting with high MELD scores.[6,7]

From the urgency point of view, patients at higher risk of dropout from the waiting list should deserve a higher priority to be transplanted. This implies that higher priority should be given to those HCC patients having greater tumor diameter, higher AFP levels, or poor response to LRT.[8]

This "approach of urgency," taking into consideration the equity in organ

access between HCC and non-HCC patients, also has some relevant limits. In fact, an urgency-based system would assign organs to patients who are most likely to drop out from the waiting list, but this approach may be in disfavor of the utility principle because patients at the greatest risk of dropout may also be the patients having the highest post-LT mortality and/or risk of HCC recurrence.[8]

To overcome the disadvantages of both the utility and urgency principles, a ''transplant benefit endpoint,'' considering pre and also post-transplant outcome, has been developed by our group. Indeed, this principle applied to the individual LT candidate has the potential to create an ideal balance between the concepts of urgency and utility.[2,7,9] Recently, we were able to demonstrate in a very large European HCC patient population that patients having the highest transplant benefit are those beyond MC, having a partial response to LRT and a low AFP level. Conversely, HCC patients obtaining a CR (ie, high utility, but low urgency) or a poor response to LRT (ie, high urgency, but low utility) have a low transplant benefit.[6]

In conclusion, this study is another important contribution to the ongoing refinement of post-LT outcome prediction in HCC patients. We are now on the edge of a revolution in which the 20-year-long monopoly of ''static'' features as reliable indicators for LT is progressively weakened this in favor of ''dynamic'' tumor characteristics such as response to therapy and AFP dynamics. The results of the study by Agiopan et al should be interpreted in the context of a more ''comprehensive transplant benefit'' vision of the complex LT allocation process. In fact, this study strongly underlines that the actual US liver transplant selection policy for patients with and without HCC is still heterogeneous. This allocation model intrinsically ''feeds'' unethical paradox in which donated organs are allocated to the ''sickest first'' in non-HCC hepatic-diseased candidates[10] and to the ''earliest first'' (ie, patients with compensated cirrhosis and CR) in HCC candidates; this choice is made irrespective of the survival prospects when applying therapies other than LT.[1]

One of the fundamental challenges of organ allocation science is maintaining (and guaranteeing) equity among the heterogeneous groups of potential liver recipients inserted on the waiting list. In the specific context of organ allocation, equity means treating all patients according to a common endpoint. In this perspective, the principle of equity outweighs all others, whether we decide to favor urgency, utility, or benefit as endpoints for our allocation system.[7]

QL and AV equally contributed to this work.

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Response: ''Which is the True Role of Bridging Therapies for HCC Patients Waiting for Liver Transplantation?''

Reply:

We very much appreciate the comments of Drs Lai, Vitale, Rossi, Cillo, and Lerut on behalf of the European Hepatocellular Cancer Liver Transplantation (ErHeCaLT) Study Group regarding our manuscript,[1] examining the effect of pretransplant bridging locoregional therapy (LRT) on recurrence of hepatocellular carcinoma (HCC) after liver transplantation (LT) in patients within Milan criteria. By virtue of examining outcomes in listed HCC patients who actually received LT, the dataset from our US Multicenter HCC Transplant Consortium (UMHTC) could only be expected to assess the utility endpoint (ie, risk of post-LT HCC recurrence). A thorough intention-to-treat analysis, as Lai et al allude to, would have allowed for a robust analysis of urgency (ie, pre-LT outcome) and transplant benefit as well; unfortunately, the UMHTC dataset does