Transplant International

FORUM

Liver transplantation for colorectal liver metastasis: aiming for a cure or a palliation?

Axel Andres[1,2], Gonzalo Sapisochin[3], Silvio Nadalin[4], René Adam[5] & Christian Toso[1]

This Forum discusses the paper by the Oslo Group: Treatment of relapse and survival outcomes after liver transplantation in patients with colorectal liver metastases. Transpl Int. 2021:34; 2205.

1 Division of Abdominal Surgery, Geneva University Hospitals, University of Geneva, Geneva, Switzerland
2 Division of Transplantation, Geneva University Hospitals, University of Geneva, Geneva, Switzerland
3 Abdominal Transplant & HPB Surgical Oncology, Toronto General Hospital, University of Toronto, Toronto, ON, Canada
4 Department of Surgery and Transplantation, University Hospital, Tübingen, Germany
5 Centre Hépato-biliaire, Assistance Publique-Hôpitaux de Paris, Paul Brousse Hospital, Univ. Paris-Sud, Villejuif, France
E-mail: axel.andres@hcuge.ch

Correspondence
Axel Andres and Christian Toso, Divisions of Abdominal Surgery and Transplantation, Geneva University Hospital, 4 rue Gabrielle-Perret-Gentil, 1211 Genève 14, Geneva, Switzerland.
Tel.: +41223727702;
fax: +41223727707;
e-mails: axel.andres@hcuge.ch (A.A.) and christian.toso@hcuge.ch (C.T.)

Accepted for publication:
25 August 2021

Transplant oncology is a field of growing interest, with increasing number of patients transplanted for cancer [1]. Among such indications, colorectal liver metastasis is under intense scrutiny considering the high number of potential new recipients. The important article by the Oslo group published in the current issue of *Transplant International* brings more light on their post-transplant fate [2].

Although 44 out of the 56 described recipients demonstrated a recurrence (93% of recipients at 24 months), more than 50% could benefit from a treatment of recurrence with curative intent. When such a treatment was applied, 5-year overall survival from the time of recurrence was 51.3%. Of interest, patients with lung recurrence demonstrated a more indolent disease (more time from transplant to recurrence), could be more often treated via a curative mean, and enjoyed an improved survival. Luckily, the lung was the most frequent site of recurrence (52.3%). A number of questions remain open:

Is transplantation better than no transplant in patients with nonresectable colorectal metastasis?

Based on the present and other nonrandomized data, transplantation patients likely enjoy longer overall survivals than those without [3]. One must keep in mind that transplanted patients with colorectal liver metastasis were highly selected, and would also likely have enjoyed an outlier prolonged survival on chemotherapy alone. Outcomes of ongoing randomized controlled studies comparing transplant versus chemotherapy are therefore needed. On top of this, quality of life after transplantation compared with 'chronic' chemotherapy is still to be explored, considering that a number of patients have undergone multiple resections after transplant. Do they spend their life in-hospital or can they, on the contrary, enjoy the years of life gained? These data combined will help confirm the quality of life-adjusted survival benefit.

Should we be more selective and aim for a cure, or accept recurrence in a palliative transplantation setting?

The Oslo group has been able to exploit their privileged situation with an excess of liver grafts in order to develop a laboratory to explore borderline transplant indications without impacting other transplant candidates. Overall five-year survival was 83% using restrictive selection criteria [4]. A cure was possible in some patients (patients free of recurrence at 5 years: 4/56 [7%] in Oslo and 3/12 [25%] in the Compagnons Hepato-biliaires group [5]). However, recurrence was almost the rule, yet often associated with long-term survival. A key question is therefore to know whether it would be better to use ultra-restrictive selection criteria and aim for a recurrence-free survival, or to be inclusive and consider recurrence almost obligatory in the management of a chronic disease, in which transplant is only one step. While access to liver grafts varies greatly

doi:10.1111/tri.14032

from one country to the other, the minimal acceptable post-transplant outcome should be adjusted accordingly. Countries with short waiting times such as Spain and the Scandinavian countries are in positions to use less restricted criteria, perform more palliative transplantation (in patients with nonresectable metastasis) and accept higher recurrence rates. It is also the case in countries were living donation represents a large proportion of available grafts (with no impact on other patients in the waiting list). However, a stepwise approach appears advisable, starting restrictive before potentially being more inclusive.

How should allocation be managed?

Another extremely difficult task is the management of the waiting list, and defining a fair prioritization. With the growing number of patients listed for oncological indications, and granted, in many countries, exception points, the MELD system is increasingly becoming obsolete. Patients listed based on lab MELD tend to be disadvantaged [6]. New allocation schemes may need to be explored, but the task will be challenging as the goal of transplantation is differing between indications. Patients with decompensated cirrhosis are at high risk of death pretransplant (urgency), but tend to do well after. Those listed for HCC are at lower risk of short-term death pretransplant, and aim for an appropriate five-year survival. Finally, those listed for colorectal metastasis are also at relatively low risk of death pretransplant, but should be seen as aiming for an appropriate five-year survival despite the presence of a 'planned' recurrence. With the potential increase in the number of listed patients with colorectal metastasis, more refined allocation policies will need to be defined. In parallel, alternative sources of liver grafts will also need to be further exploited (extended, live, domino, RAPID).

Overall, the field of transplantation for colorectal metastasis is moving fast, and the Oslo team must be thanked for taking the lead. A number of challenges are lying ahead, including defining whether 'palliative' transplantation (with almost planned recurrences) is acceptable, and improving graft allocation. These challenges will require a high number of patients treated at different centres in order to avoid the overfitting linked to the specificity of a single centre. In this aim, pooling data in an international registry would undoubtedly accelerate our insight in this topic.

Funding

Open access funding provided by Universite de Geneve. WOA Institution: Universite de Geneve Blended DEAL: CSAL.

REFERENCES

1. Sapisochin G, Hibi T, Toso C, *et al.* Transplant oncology in primary and metastatic liver tumors: principles, evidence, and opportunities. *Ann Surg* 2021; **273**: 483.
2. Oslo Group. Treatment of relapse and survival outcomes after liver transplantation in patients with colorectal liver metastases. *Transplant Int* 2021; **34**: 2205.
3. Dueland S, Yaqub S, Syversveen T, *et al.* Survival outcomes after portal vein embolization and liver resection compared with liver transplant for patients with extensive colorectal cancer liver metastases. *JAMA Surg* 2021; **156**: 550.
4. Dueland S, Syversveen T, Solheim JM, *et al.* Survival following liver transplantation for patients with nonresectable liver-only colorectal metastases. *Ann Surg* 2020; **271**: 212.
5. Toso C, Pinto Marques H, Andres A, *et al.* Liver transplantation for colorectal liver metastasis: survival without recurrence can be achieved. *Liver Transpl* 2017; **23**: 1073.
6. Ishaque T, Massie AB, Bowring MG, *et al.* Liver transplantation and waitlist mortality for HCC and non-HCC candidates following the 2015 HCC exception policy change. *Am J Transplant* 2019; **19**: 564.