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Review Article

Liver transplantation for intestinal malignancies

Alessandro Vitale[a,*], Gabriel Gondolesi[b], Michele Finotti[c], Clarissa De Nardi[a], Chiara Naldini[a], Edoardo G Giannini[d], Francesco D'Amico[e]

[a] Department of Surgical, Oncological, and Gastroenterological Sciences, Padua University, Padova, Italy
[b] Medstar Georgetown Transplantation Institute, Medstar Georgetown University Hospital. 3800 Reservoir Road, WA DC 20016, USA
[c] Klinik für Allgemeine, Viszeral- und Transplantationschirurgie, Universitätsklinikum Tübingen, Tübingen, Germany
[d] Gastroenterology Unit, Department of Internal Medicine, University of Genoa, Genoa, Italy
[e] Department of Precision and Regenerative Medicine and Ionian Area, Hepatobiliary Surgery and Liver Transplant Unit, University of Bari Aldo Moro, Bari, Italy

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ABSTRACT

Liver transplantation (LT) is increasingly recognised as a valuable treatment option in carefully selected cases of metastatic intestinal cancers. While traditionally reserved for primary liver tumours such as hepatocellular carcinoma (HCC), recent evidence has broadened the transplant oncology paradigm to include colorectal liver metastases (CRLM) and neuroendocrine liver metastases (NELM). This review explores the evolving indications, patient selection criteria, and clinical outcomes of LT in these contexts, emphasising the need for a conceptual and methodological reassessment.

We distinguish between prognostic factors, which are variables independently linked with clinical outcomes, and selection criteria, which determine patient eligibility and transplant prioritisation. This distinction is vital for proper candidate stratification.

It emphasises the importance of using overall survival as the primary endpoint in transplant oncology rather than recurrence-free survival, which can be misleading due to early detection bias and competing risks. The idea of "transplant benefit," defined as the survival gain attributable to LT compared to non-transplant strategies, is proposed as a fair and informative measure for ethical allocation. Data from prospective studies, such as SECA I–II and the TransMet trial, offer estimates of benefit in different indications, showing significant variation, from 22.5 months in per-protocol CRLM to around 12 months in NELM. We also examine intention-to-treat versus per-protocol analyses, the impact of dropout and waiting list mortality, and the implications for allocation policy.

Finally, we outline future directions, including expansion to unresectable tumours beyond the criteria and borderline resectable tumours within the criteria. In the era of personalised medicine, LT for intestinal malignancies requires careful patient selection, transplant ethics, and collaborative oncologic governance.

1. The concept of transplant oncology: expanding the frontier to intestinal malignancies

The evolving field of transplant oncology [1] is redefining the boundaries of organ transplantation by integrating oncological principles into the selection, timing, and strategy of liver transplantation (LT). Well-established for hepatocellular carcinoma (HCC) [2], the concept now extends to select cases of intestinal malignancies, particularly colorectal liver metastases (CRLM) and neuroendocrine liver metastases (NELM), marking a shift from the traditional paradigm.

This shift challenges conventional contraindications and aims to incorporate LT into multidisciplinary cancer care algorithms, emphasising biological tumour behaviour and patient-specific prognostic factors rather than solely anatomical resectability, and increasing transplant applicability [3].

Colorectal cancer is one of the most common malignancies worldwide, and over 50 % of patients eventually develop liver metastases. Unfortunately, the majority of these (up to 80 %) are considered unresectable due to an extensive tumour burden, unfavourable distribution, or comorbidities [4,5]. In such cases, systemic therapy remains the primary treatment. Yet, the 5-year overall survival (OS) rarely exceeds 15 %—a stark contrast to the

* Corresponding author at: Department of Surgical, Oncological and Gastroenterological Sciences, University of Padova, Padova, Italy.
E-mail addresses: alessandro.vitale@unipd.it (A. Vitale), egiannini@unige.it (E.G. Giannini).

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promising results emerging from LT in highly selected CRLM cohorts. In the SECA trials and more recently in the TransMet randomised controlled trial, LT demonstrated a significant survival benefit in selected patients, establishing its potential as a curative strategy in cases with favourable tumour biology [6–9].

Neuroendocrine neoplasms (NENs), although relatively rare, often metastasise to the liver, mainly when originating from the gastrointestinal tract. NENs generally follow a more indolent course [10]. As a result, aggressive locoregional therapies, including hepatic resection, ablation, or arterial embolisation, often remain effective and favoured by the oncologists. However, in the subset of patients with unresectable liver-dominant disease that resists medical and interventional treatments, LT becomes a viable option. Evidence from retrospective series and expert consensus evolved over time, suggesting that LT in this context can provide excellent long-term survival, with 5-year OS exceeding 70 % in patients selected according to the Milan criteria [11–13].

The decision to offer LT for intestinal malignancies depends not only on technical feasibility but also on ethical and resource considerations. CRLM is a common condition, but transplantation remains a rare indication due to strict selection criteria and organ allocation limitations, which have been addressed by using living donors. Conversely, NELM remains a rare disease and an equally rare indication for transplantation.

Although these indications remain restricted, they demonstrate the potential of transplant oncology to transform the treatment landscape for metastatic gastrointestinal cancers.

Other malignancies, such as gastrointestinal stromal tumours (GISTs), have been examined in exceptional cases but currently lack sufficient evidence to support routine transplant-based approaches [14].

This review aims to explore the rationale, current evidence, and future prospects of LT in intestinal malignancies, focusing on CRLM and NELM as primary candidates for transplant oncology. By critically analysing patient selection, trial data, and comparative survival models, we seek to define the boundaries of transplant benefit within this emerging field.

2. The ethical sustainability of liver transplantation for intestinal malignancies

The increasing use of LT for certain patients with non-hepatocellular intestinal cancers, particularly unresectable CRLMs and NELMs, raises significant ethical questions about organ allocation, fairness, and societal benefit. Although these indications remain rare and debated, they are becoming more recognised within transplant oncology, especially when rigorous patient selection and survival benefits are demonstrated [11].

Historically, ethical concerns have arisen from the idea that offering LT to new oncologic patients might restrict access for individuals with traditional indications, such as end-stage liver disease or HCC [11,15]. This tension is particularly evident in the context of deceased donor liver transplantation (DDLT), where organ scarcity remains a worldwide issue.

The next ethical consideration discussed was the survival benefit. This issue became even more significant because the lack of prioritisation led programs to use living donors, raising concerns about the ethics related to donor risk and recipient survival benefit. In 2001, when living donors were considered an option for patients with HCC beyond the Milan criteria, a 50 % recipient survival rate at 5 years was regarded as adequate to proceed [16,17].

While the rarity of NELMs as clinical entities causes minimal concern regarding their effect on the already limited donor organ supply [11], greater concern arises from the significant epidemiological burden caused by CRLM, which are among the leading causes of cancer-related death worldwide [18]. In this context, recent data and models help redefine the ethical debate by assessing the actual impact of including highly selected CRLM patients in transplant programmes [19]. These models show that when strict selection criteria are applied, such as excluding patients with general contraindications to LT (e.g., advanced age, severe comorbidities), and those with confirmed technical unresectability, as well as favouring tumours with better biology, the proportion of CRLM patients eligible for LT decreases significantly, in general every four patients evaluated in a given program with CRLM, only one will qualify for listing. According to the funnel model from Dueland et al., only 1–2 % of the current liver transplant volume would be additionally needed to accommodate CRLM candidates under strict criteria [19]. This model challenges the perception of CRLM as a disruptive burden to organ allocation, but until this concept is fully understood worldwide, living donation becomes the only alternative to do timely transplants in those accepted candidates (except countries with a superior number of deceased donors).

Conversely, the traditional 'Titanic' paradigm, where LT was viewed as an overloaded therapeutic ocean liner with too few lifeboats (organs) for its many passengers (patients), is transforming. Advances in surgical techniques and organ preservation are gradually reducing the constraints caused by organ scarcity.

The increased use of LDLT and the implementation of in-situ and ex-situ perfusion technologies have significantly expanded the donor pool and improved graft preservation, consistently contributing to a measurable increase in transplant volumes in both Europe and North America [20] (Fig. 1), suggesting that ethical concerns must be considered within a dynamic and growing system and providing opportunities to broaden transplant indications safely. Robotic donor hepatectomy is proving to be safe and feasible, fostering greater acceptance of LDLT even in centres without extensive laparoscopic experience [21]. Meanwhile, machine perfusion technologies (both in situ and ex situ) are transforming the landscape of organ viability assessment and reconditioning [22,23]. These advancements enhance the feasibility of applying LT in oncological settings without necessarily restricting access for standard indications.

In summary, LT for intestinal malignancies, especially for CRLM and NELM within strict criteria, can be ethically justified when it follows principles of benefit maximisation, fair allocation, and scientific rigour.

3. History of liver transplantation for intestinal malignancies

LT for metastatic intestinal cancers has evolved from sporadic, experimental procedures into a well-established, evidence-based therapeutic option for certain patients. Early efforts, especially from the 1980s to the late 1990s, were characterised by high perioperative mortality and a lack of clear selection criteria. These initial experiences led to poor outcomes, resulting in the discontinuation of LT in metastatic cases for many years [3,11].

3.1. CRLM: A two-step revolution, SECA's vision and transmet's validation

Before the introduction of modern selection criteria, LT for CRLM was carried out sporadically, often with poor outcomes.

Data from the European Liver Transplant Registry (ELTR) reported 58 transplants for CRLM up to 2007, with the majority performed before 1995, and 5-year survival rates as low as 18 % [5,24]. These early cases occurred when LT was considered experimental and lacked biological or clinical stratification. But a later review of lymph nodes of the cases done by Mullbacher et al. in 1991 [5], showed that 15/21 initially classified as negative, in reality did have micrometastasis, therefore when they review the long

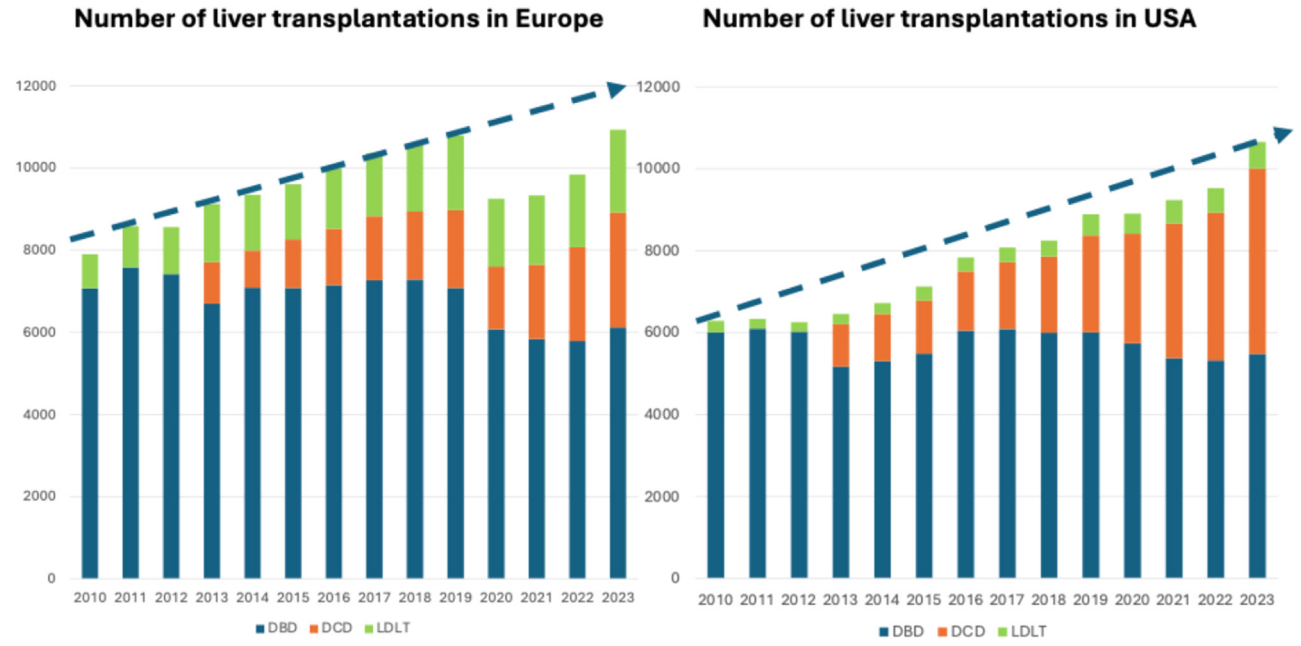

Fig. 1. Increasing number of liver transplants in Europe and the United States. DBD, brain dead donors. DCD, donation after cardiac death donors. LDLT, living donor liver transplantation.

term freedom from recurrence survival on those with real negative lymph nodes it was 118 months, vs 28 months for those with positive nodes ($p = 0.01$), highlighting the importance of restric criterias – and adequate pathology reading-, even then.

The following key step in the history of LT for CRLMs was the SECA I trial (Oslo group, 2006–2011), which showed a 5-year OS of 60 % in carefully selected patients, despite high recurrence rates [6]. This revived interest in transplant oncology for CRLM and led to SECA II, which improved selection criteria based on tumour biology, response to chemotherapy, and the absence of extrahepatic spread [25]. The most favourable subgroup (Oslo score 0–2) achieved 5-year survival rates of about 63 % and a 10-year OS of around 46 %, matching standard indications for transplantation [7,8]. A notable shift in transplant oncology took place with the publication of the TransMet trial, the first randomised controlled study with a sufficient sample size in this field [9]. For the first time, LT for CRLMs shifted from an experimental procedure to a recognised oncological indication. In the per-protocol analysis, LT achieved an overall 5-year survival rate of 73 % compared to only 9 % in the chemotherapy arm, providing strong level I evidence in favour of transplantation for selected patients.

In summary, the trajectory of LT for intestinal malignancies demonstrates a shift from high-risk salvage therapy to a treatment based on biological selection and increasing evidence. The key milestones in both CRLM and NELM transplantation emphasise the essential importance of patient selection, multidisciplinary assessment, and survival benefit.

3.2. NELM: from salvage therapy to selective indication

Liver transplantation was proposed for NELMs in 1988 by O'Grady et al., who reported 8 cases; their recommendation was not to proceed until more stringent criteria could be established [26]. In the first era, LT was performed on patients with NELM, aiming for the complete removal of macro- and micro-NELMs. However, the prognosis during this earlier period was unsatisfactory, with 5-year OS and RFS rates of approximately 50 and 30 %, respectively [27].

Indications extend further by considering the possibility of performing modified multivisceral transplants in locally advanced lesions without liver metastasis or using liver-containing intestinal transplants in selected patients. Isolated cases of multivisceral or modified multivisceral transplantation (MVT) in patients with extensive mesenteric disease or tumours of the pancreatic head have been performed. Although technically feasible, MVT remains limited to small case series and select institutional cohorts, and its role is now mostly confined to exceptional, non-metastatic cases in experienced centres [28].

The paradigm began to shift with the introduction of the Milan criteria in 2007 [29], which established strict selection standards for patients with NELM: age <60 years, well-differentiated tumours (G1–G2), resected primary tumour with portal drainage, no extrahepatic disease, <50 % liver involvement, and disease stability for ≥6 months. This marked a turning point: prospective application of these criteria showed 5-year overall survival rates exceeding 90 %, prompting the formal inclusion in international guidelines [30,31]. Retrospective series and multicentre studies confirmed the long-term efficacy of LT in this highly selected cohort [32,33].

4. Prognostic factors and selection criteria in transplant oncology

4.1. Methodological foundations

In transplant oncology, recognising the difference between prognostic factors and selection criteria is both conceptually and clinically vital.

Prognostic factors are variables that are independently associated with clinical outcomes, such as overall survival or disease recurrence, regardless of the treatment administered. They are usually identified through multivariable analyses within large observational datasets and help in estimating the natural progression of the disease. For instance, high CEA levels or the presence of right-sided colorectal cancer have been demonstrated to affect survival after LT for CRLM [34,35].

Selection criteria, on the other hand, are practical tools used to evaluate patient eligibility for specific therapies. These may include

prognostic factors but also encompass clinical, logistical, and sometimes empirical elements. Early in the development of a new transplant indication, such as LT for HCC or CRLM, selection criteria are often based on expert consensus, case series, or pathophysiological reasoning. For example, the Milan criteria, derived initially from a small prospective study in HCC, have served as a key selection tool, despite their predictive limitations [36,37].

A key distinction is that prognostic factors are statistically validated indicators of outcome. In contrast, selection criteria serve as gatekeeping thresholds, often employed to enhance utility and fairness in resource distribution, especially in cases of organ scarcity [34,38,39].

As the clinical use of transplant indications progresses, a methodological development is anticipated. Three stages can be identified.

An initial exploratory phase: selection criteria are based on preliminary evidence and expert opinion. A validation phase: larger registries and multicentre cohorts enable the derivation of robust prognostic factors. A personalised transplant phase: predictive models incorporating both survival outcomes and treatment options (e.g., transplant benefit versus chemotherapy) are developed [9,40,41]. In this final phase, it becomes increasingly important to distinguish between prognostic and predictive factors [42]. While prognostic factors indicate likely outcomes, predictive factors suggest differential responses to treatment options. Not all selection criteria are prognostic, and not all prognostic variables are predictive or incorporated into the selection process (Supplement Table 1). For instance, female sex was recently associated with worse survival after LT for CRLM but has not yet been adopted into selection algorithms [35].

Selection criteria become essential for listing criteria, but prognostic factors might be used to establish priority for accessing a deceased donor.

4.2. Prognostic and selection variables in LT for CRLMs and NELMs

LT for CRLM and NELM necessitates strict patient selection to optimise outcomes and ensure responsible organ allocation. Table 1 summarises and contrasts the established selection criteria with the emerging prognostic factors proposed for each condition, reflecting the growing evidence base and the biological differences in the diseases.

In CRLM, selection criteria are primarily based on evidence from the SECA trials [6,25] and further refined by the TransMet study [9], focusing on factors such as liver-only disease, durable response to chemotherapy, low CEA levels, and the absence of high-risk molecular markers (e.g., BRAF mutation). These factors not only predict favourable outcomes after transplantation but also indicate the potential for significant control through surgery. However, recent multicentre data have identified additional variables that may independently influence prognosis, regardless of their inclusion in current selection algorithms [35]. Female sex, right-sided primary tumours, and elevated CEA levels have emerged as independent predictors of poor post-transplant survival in multivariate analyses, emphasising the need to update existing frameworks based on larger datasets and predictive modelling.

In contrast, selection criteria for NELM have been traditionally based on expert consensus (e.g., Milan criteria) [29–31]. They emphasise indolent tumour biology, the absence of extrahepatic spread, and sustained disease control. Prognostic refinement in NELM remains limited due to the relatively small number of transplant cases. However, poor differentiation (G3), a high Ki-67 index, and PET positivity are repeatedly associated with worse outcomes in retrospective analyses [11]. This distinction between formal eligibility criteria and genuine prognostic variables emphasises the significance of continual refinement, moving from expert-based

Table 1
Selection Criteria vs. Prognostic Factors in LT for CRLM and NELM.

Category	CRLM	NELM
Selection Criteria		
- *Controlled primary tumor*	R0 resection of colorectal primary	R0 resection of neuroendocrine primary (pancreatic/small bowel)
- *Disease confined to liver*	Absence of extrahepatic disease confirmed by PET-CT	No extrahepatic disease (confirmed by PET-CT or somatostatin imaging)
- *Response to therapy*	Disease control (stable/partial response) ≥6 months before LT	Stable disease ≥6 months after systemic therapy
- *Tumor burden*	Largest lesion ≤5.5 cm; number of lesions typically <10	Liver involvement ≤50 % (Milan criteria)
- *Tumor markers*	CEA ≤80 µg/L	Low/moderate chromogranin A; no high proliferation index
- *Molecular features*	Absence of BRAF V600E; MSS (non-MSI-high); RAS wild-type preferred	G1/G2 NET (well to moderately differentiated); Ki-67 < 20 %
- *Age (some protocols)*	Preferably <65 years	Age <60 (Milan criteria); biologic age considered
Prognostic Factors		
- *Demographics*	Female sex associated with worse post-LT survival (recent multivariable data)	Younger age favorable; sex not clearly prognostic
- *Tumor biology*	Right-sided primary CRC associated with worse prognosis	G3 or poorly differentiated NET associated with worse survival
- *Tumor burden*	Number >10 and diameter >5.5 cm associated with lower survival	Involvement >50 % of liver associated with higher recurrence risk
- *Biomarkers*	CEA >80 µg/L and KRAS mutations associated with worse outcomes	High Ki-67 index and high chromogranin A are negative predictors
- *Disease kinetics*	Disease progression on chemotherapy = contraindication; short time from primary tumor resection to LT	Rapid progression before LT associated with poor outcomes
- *Other*	Prior liver-directed therapy may be protective Metabolic tumour volume	Post-LT recurrence risk linked to microscopic residual disease, PET avidity

rules towards evidence-based, personalised risk models. As transplant oncology evolves, integrating multivariate prognostic tools into selection procedures will be essential to maximise survival advantages and promote fair resource distribution.

5. Endpoints and allocation criteria

5.1. Overall survival vs. recurrence-free survival in transplant oncology

In transplant oncology, especially in liver transplantation (LT) for intestinal malignancies, selecting appropriate clinical endpoints significantly impacts patient selection, trial design, and post-transplant assessment. While recurrence-free survival (RFS) has traditionally been used to evaluate oncologic treatments, it can be misleading in the LT setting. RFS typically counts tumour recurrence as an event (while death is censored) but does not differentiate between lethal and non-lethal recurrences.

Conversely, overall survival (OS) remains the most reliable and patient-centred endpoint in this context. This is demonstrated in Fig. 2A–C, which compare OS and RFS in three key transplant oncology indications: CRLMs, NELMs, and HCC. Despite the high recurrence rate after LT for CRLM, patients often survive for a long time with controlled disease, highlighting the importance of prioritising OS over RFS when assessing the effectiveness of LT in these conditions.

5.2. Allocation principles: utility, urgency, and transplant benefit

Three main principles guide organ allocation in transplant oncology [43]. Utility focuses on maximising post-transplant outcomes. Under this criterion, LT for NELM would be prioritised over CRLM due to superior post-transplant survival metrics, as shown in multiple studies [8,33].

Urgency addresses the risk of mortality without a transplant. Patients with CRLM generally experience higher dropout rates and lower survival rates without LT compared to NELM, thus favouring prioritisation under this principle [9,32].

The transplant benefit combines both principles mentioned earlier, defined as the survival advantage of LT compared to the best alternative therapy. Recent data indicate that the 5-year transplant benefit from the day of LT is: 22.5 months for CRLM [9] (Fig. 3) and 12.8 months for NELM [32]. This combined concept of transplant benefit offers a fairer basis for resource allocation [44].

A graph in Fig. 4 shows the 5-year transplant benefit across various transplant oncology indications using histograms. Notably, transplant benefit values for CRLM and NELM were compared with those of LT for HCC under specific conditions [45,46].

If we aim to achieve those results, the next ethical question will be whether it is justifiable to perform re-transplantation on patients with recurrent hepatitis C cirrhosis, while denying patients with CRLM or NELM a liver transplant, knowing that the outcome is at least similar, if not better.

5.3. Per-Protocol vs. intention-to-treat analysis

A crucial methodological aspect in transplant oncology is the definition of the analytical cohort used to estimate transplant benefit. While intention-to-treat (ITT) analysis includes all patients at the time of listing—thereby accounting for dropouts and waitlist mortality—its applicability is limited by external factors such as local organ availability, listing policies, and disparities in access to transplant. These confounding variables, often unrelated to tumour biology or treatment efficacy, may distort comparisons between indications.

In contrast, the per-protocol (PP) analysis, which only considers patients who underwent LT, enables a more controlled and biologically meaningful comparison across oncological indications. This is especially valid in research settings or model-based allocation frameworks where access to transplants is standardised.

The TransMet trial [9] illustrates this: the 5-year transplant benefit for CRLM was 22.5 months in the per-protocol cohort (Fig. 3), compared to 12.5 months in the ITT population. However, the ITT estimate was influenced by patients in the chemotherapy arm who ultimately underwent resection or even transplant after a positive treatment response, thereby artificially boosting non-transplant survival.

Therefore, the benefit of transplant under the per-protocol approach should be prioritised when aiming to compare oncological transplant indications fairly, especially when selection criteria, perioperative risks, and biological behaviour are the main factors of interest. We also need to recognise that no randomised clinical trials or intention-to-treat analyses have been conducted by the transplant community to validate Milan criteria or to perform liver transplantation in HCC beyond the accepted criteria.

6. Expanding the transplant oncology criteria: beyond and within

The future of transplant oncology relies on refining, not discarding, the core principles that guide current indications. One such principle is non-resectability, which supports accepted transplant indications for CRLM (e.g., SECA/TransMet criteria) and NELM (Milan criteria). However, as our understanding of tumour biology and treatment pathways progresses, two potential categories of expansion are emerging.

6.1. Unresectable beyond criteria

This group consists of patients who meet the essential condition of non-resectability, but whose tumour features fall outside the current selection criteria—for instance, due to excessive tumour burden, borderline biological markers, or a treatment response shorter than 6 months. These cases are discussed in Fig. 5A-B, where the transplant benefit is projected to be well below 10 months at 5 years, indicating a modest survival advantage [9,47–49].

6.2. Borderline resectable within criteria

In contrast, this second group comprises patients who meet all standard biological and morphological criteria for LT but are considered technically resectable, though with a high operative risk or an unfavourable prognosis after LR [50]. The issue is not a lack of resectability itself but the expectation that LT might provide better oncological outcomes. As Fig. 5C-D illustrate, the potential transplant benefit in these cases can be significant, especially in CRLM (up to 20 months), and more moderate in NELM (approximately 8 months) [33,48].

These two models reflect different strategic directions: the former tests the outer limits of selection safety, while the latter questions the clinical value of resectability as a binary endpoint.

6.3. Ethical sustainability and donor strategies

Expanding indications raise ethical concerns, particularly regarding organ allocation. However, innovative strategies like LDLT and RAPID offer a framework to ethically explore these extensions without impacting standard indications. LDLT and RAPID have already shown feasibility in pilot cases and may mitigate waiting list

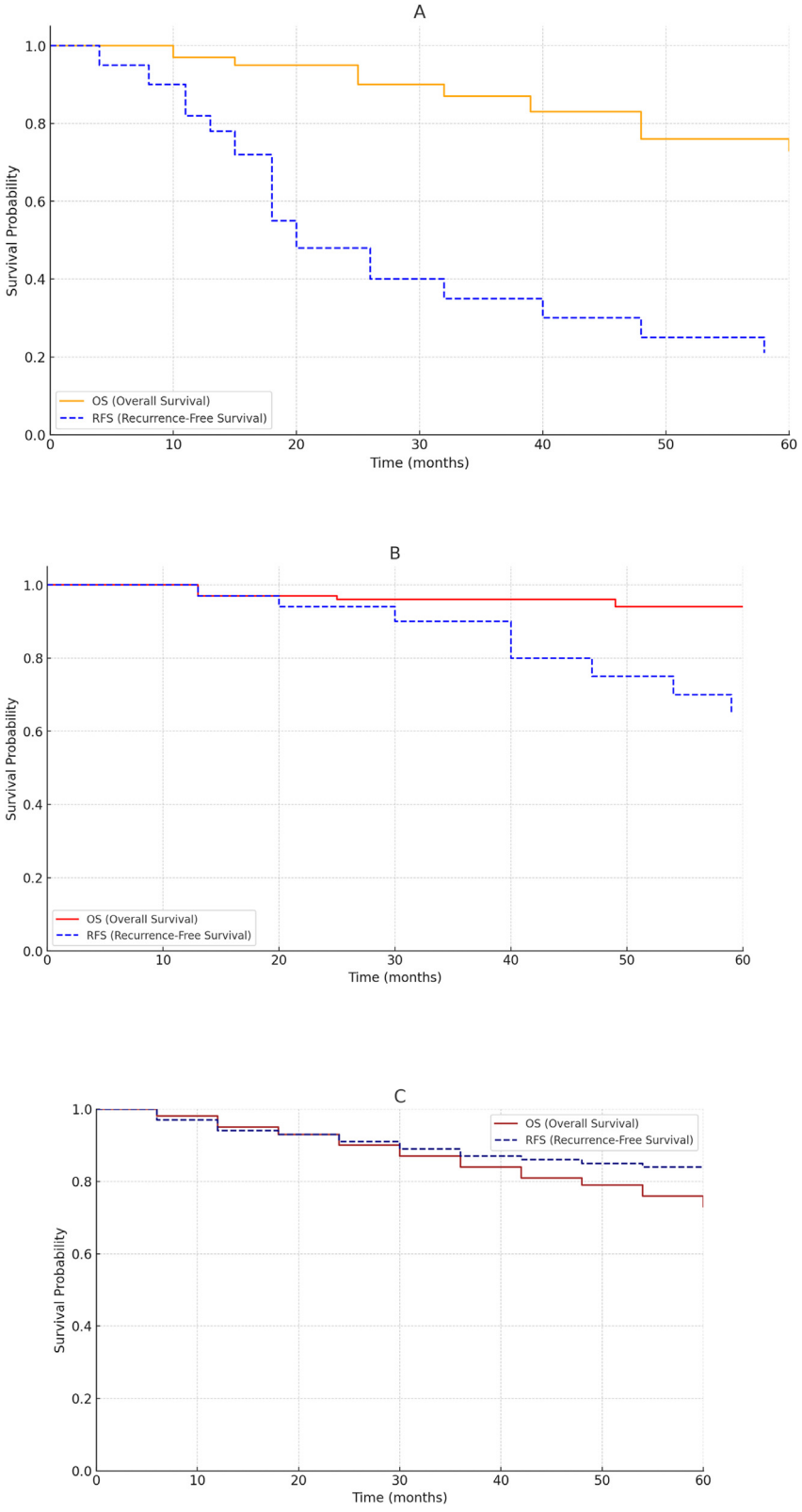

Fig. 2. Overall Survival (OS) and Recurrence-Free Survival (RFS) after Liver Transplantation for Cancer.
(A) Kaplan-Meier curves of OS and RFS in patients with colorectal liver metastases (CRLM) randomised to liver transplantation in the per-protocol arm of the TransMet study.
(B) Kaplan-Meier curves of OS and RFS in patients undergoing liver transplantation for neuroendocrine liver metastases (NELM) within the Milan criteria.
(C) Kaplan-Meier curves of OS and RFS in patients transplanted for hepatocellular carcinoma (HCC) fulfilling Milan criteria.
RFS (Recurrence-Free Survival) represents the duration until recurrence, with deaths censored, as outlined by the protocol in each dataset. OS denotes the period from transplantation to death from any cause. All time axes are truncated at 60 months for consistency.
The original survival curves were digitised using the software "Engauge digitiser," and the resulting coordinates were employed to reconstruct the individual survival data of TransMet patients. This method was developed by Guyot et al. [53] .

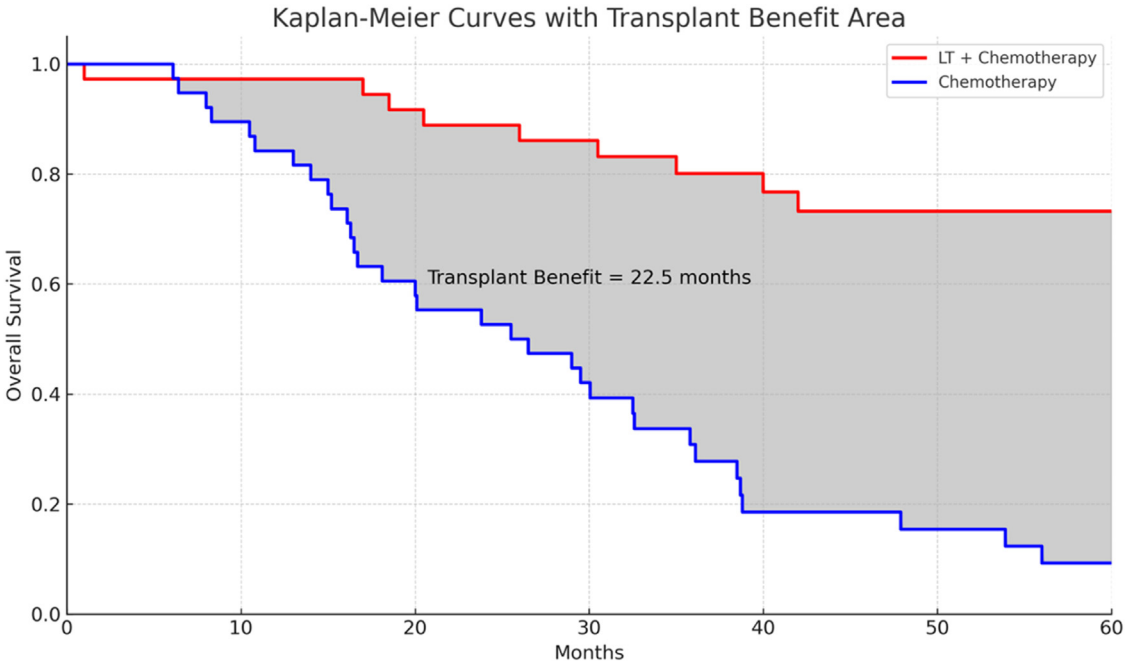

Fig. 3. Kaplan–Meier Survival Curves and Transplant Benefit in the TransMet Trial (Per-Protocol Analysis) [9]. Overall survival curves for patients with CRLM enrolled in the TransMet trial, comparing the LT plus chemotherapy (LT+CT) arm versus the chemotherapy-only (CT) arm, analysed per-protocol. The shaded grey area illustrates the transplant benefit, defined as the difference in restricted mean survival time (RMST) between the two groups over a 5-year period. The estimated transplant benefit is 22.5 months.
The survival curves of the TransMet study were digitised using the software "Engauge digitiser," and the resulting coordinates were employed to reconstruct the individual survival data of TransMet patients. This method was developed by Guyot et al. [53] The 5-year transplant benefit was then calculated as the difference between the areas under the Kaplan-Meier survival curves, truncated at 5 years, and expressed in life-expectancy months. The area under the curve was determined using the restricted mean survival time, which was limited to up to 5 years.
Abbreviations: LT, liver transplantation; CT, chemotherapy; CRLM, colorectal liver metastases; RMST, restricted mean survival time.

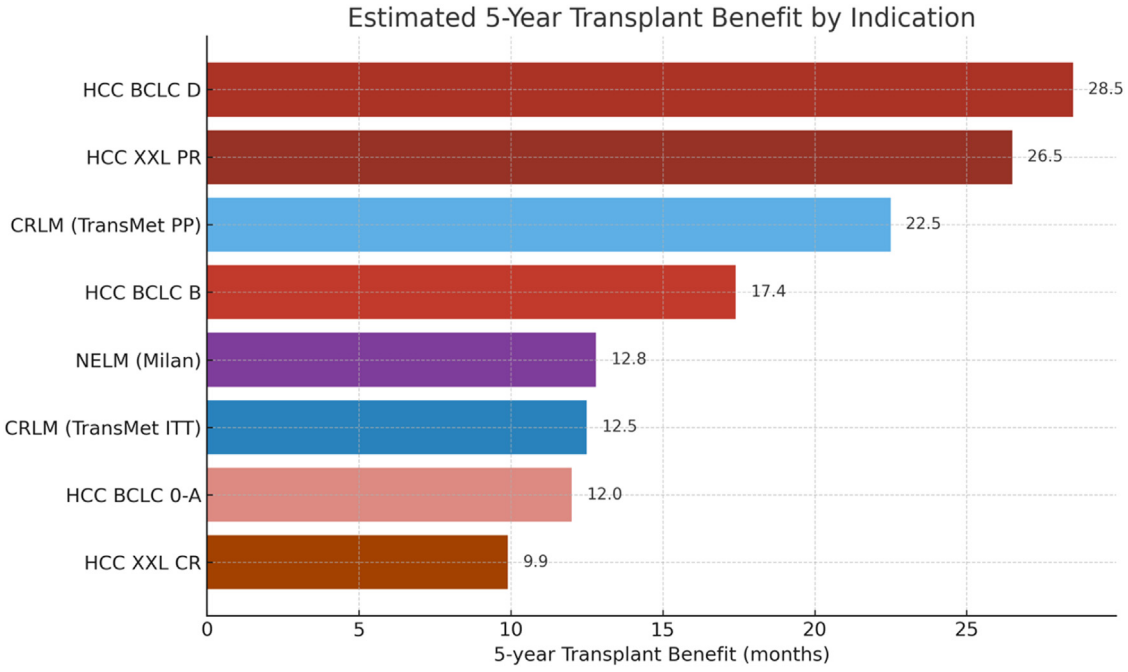

Fig. 4. Five-year Transplant Benefit (in months) across oncologic indications.
Bar chart showing the estimated 5-year transplant benefit (measured as the difference in survival months between transplanted and non-transplanted patients) for selected indications in transplant oncology. These estimates are based on comparative survival models (per protocol or intention-to-treat, as appropriate).
The chart emphasises the variability in expected benefits, with the largest gains seen in HCC BCLC D (28.5 months) and HCC XXL with partial response (26.5 months), and smaller gains in cases such as HCC XXL with complete response (9.9 months). This visualisation aids in framing discussions on fairness in allocation and the utility of transplantation.

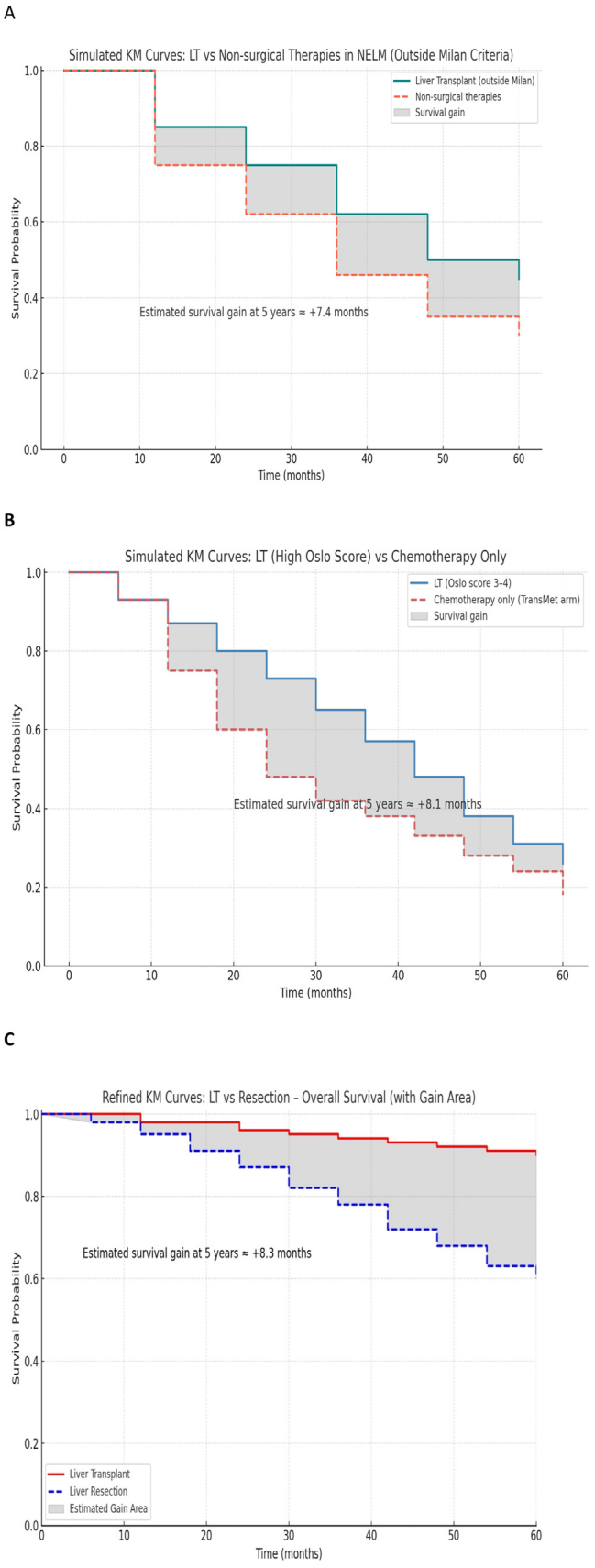

Fig. 5. Simulated survival curves and 5-year transplant benefit estimations from the recent literature. A) Unresectable Beyond Criteria NELM [47,49]; B) Unresectable Beyond Criteria CRLM [9,48]; C) Borderline Resectable Within Criteria NELM [33]; D) Borderline Resectable Within Criteria CRLM [48].

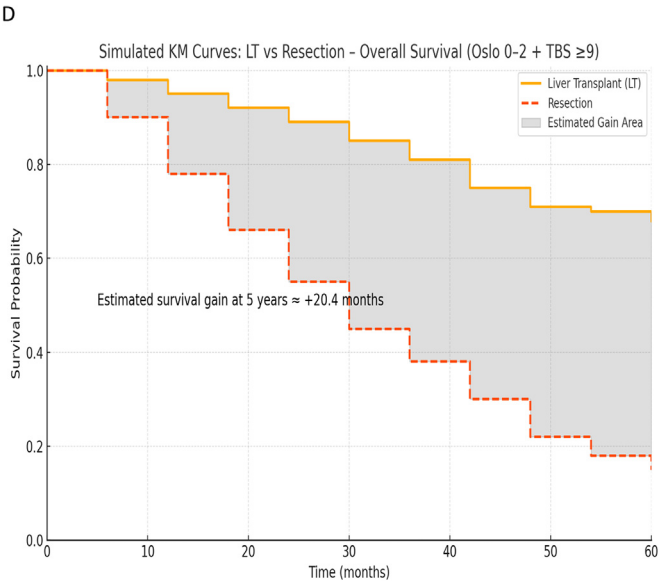

Fig. 5. Continued

pressure [51]. When new policies are discussed for adoption, decisions should be based on clear data, and if such data is unavailable, it must be generated. Rejecting it simply because it might affect transplant eligibility for non-cancer patients prevents those patients from benefiting from the currently proven, superior alternative.

7. Conclusions

LT for intestinal malignancies has advanced from experimental stages to become a well-established option in carefully selected patient groups. The integration of oncologic principles and transplant strategies has enabled the safe expansion of indications, especially for CRLM and NELM. Central to this progress is the implementation of biologically informed selection criteria, reliable endpoints such as overall survival, and quantitative models assessing transplant benefit. These methods help balance utility, urgency, and fairness in organ allocation.

Emerging data support not only the current indications but also suggest that expansion to borderline resectable cases, particularly within established criteria, may provide a significant survival advantage. Conversely, cases that exceed these criteria and are unresectable remain investigational due to limited benefits. The increasing role of living donor liver transplantation and innovative graft utilisation techniques, such as the RAPID approach, further endorse the ethical feasibility of these strategies.

Moving forward, transplant oncology must be guided by rigorous clinical trial design, predictive modelling, and ethical considerations. Through multidisciplinary collaboration [52], liver transplantation can increasingly occupy a strategic role in the treatment algorithms of selected metastatic intestinal cancers.

Declaration of competing interest

AV has received consulting fees from AstraZeneca, and Roche.

EGG reports AbbVie, EISAI, Gilead, and Roche: speaking and teaching. Ipsen: advisory board.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.dld.2025.08.008.

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