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ORIGINAL ARTICLE – HEPATOBILIARY TUMORS

# Severe Preoperative Symptoms Delay Readiness to Return to Intended Oncologic Therapy (RIOT) After Liver Resection

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## ABSTRACT

**Background.** Symptom burden, as measured by patient-reported outcome (PRO) metrics, may have prognostic value in various cancer populations, but remains underreported. The aim of this project was to determine the predictive impact of preoperative patient-reported symptom burden on readiness to return to intended oncologic therapy (RIOT) after oncologic liver resection.

**Methods.** Preoperative factors, including anthropometric analysis of sarcopenia, were collected for patients undergoing oncologic liver resection from 2015 to 2018. All patients reported their preoperative symptom burden using the MD Anderson Symptom Inventory, Gastrointestinal version (MDASI-GI). Time to RIOT readiness was compared using standard statistics.

**Results.** Preoperative symptom burden was measured in 107 consecutive patients; 52% had at least one moderate symptom score and 21% reported at least one severe score. Highest rated symptoms were fatigue, disturbed sleep, and distress. For patients reporting a severe preoperative symptom burden, the median time to RIOT readiness was 35 days (interquartile range [IQR] 28–42), compared with 21 days (IQR 21–28) for those without severe symptoms ($p < 0.001$). On multivariable analysis, severe preoperative symptom burden was independently associated with longer time to RIOT readiness (estimate +7.5 days, 95% confidence interval 2.6–12.3; $p = 0.002$).

**Conclusions.** Preoperative symptom burden has a substantial impact on time to RIOT readiness, leading to, on average, a 7-day delay in RIOT readiness compared with patients without severe preoperative symptoms. Identifying and targeting severe preoperative symptoms may hasten recovery and improve time to necessary adjuvant therapies.

For patients undergoing oncologic surgery, postoperative adjuvant therapies are often required. The ability of a perioperative care plan to recover cancer patients to the point that they can return to intended oncologic therapy (RIOT) is therefore valuable. RIOT is a newly defined quality metric that objectively measures recovery after oncologic surgery based on the ability of a patient to receive other necessary treatments after an operation.[1] Preliminary studies have determined that reporting of RIOT metrics is feasible and that failure to RIOT is associated with shorter overall survivals.[1–3] Factors such as minimally invasive surgical approach and use of an enhanced recovery pathway, have been shown to shorten time to RIOT;[1,3] however, there is currently little information on what preoperative patient factors may impact RIOT.

Previous publications have explored the predictive capability of variables such as age, comorbidities, performance status, and body composition on patient outcomes after gastrointestinal surgery for malignancy.[4–8] Sarcopenia, defined as 'a progressive loss of skeletal muscular mass' has been shown in some studies to correlate with postoperative morbidity and mortality after

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hepatopancreatobiliary (HPB) surgery, but critics note that some studies have not found this association and that sarcopenia may not be a remediable factor.[9–11] More recently, patient-reported outcomes (PROs) have also been incorporated into medical and surgical oncology risk models,[3,12–14] after numerous medical studies have suggested that PROs are predictive of clinical outcomes in various cancer populations.[15–18] In contrast to traditionally assessed risk factors, PROs are more patient-centric, more dynamic, and therefore potentially more modifiable.

A deeper understanding of the associations that PROs have with recovery after oncologic resection, where surgery may be only one of many necessary treatment modalities, could have a substantial impact on quality of life and overall survival. A recent publication from our institution suggested that patient-reported symptom burden may be one of the only preoperative factors associated with readiness to RIOT after liver surgery.[14] Thus, the aim of this research study was to further examine this relationship by determining the impact of PROs on RIOT readiness after liver surgery for malignancy in a larger cohort, with the hypothesis that the presence of severe symptoms preoperatively would be associated with delayed postoperative readiness to return to other necessary treatments.

## METHODS

### *Study Setting and Participants*

Consecutive patients undergoing liver resection at MD Anderson Cancer Center from January 2015 through December 2018 who completed the preoperative PRO tool were identified from a prospectively maintained hepatobiliary surgery database. Patients who were determined at the time of surgery to be oncologically unresectable were included and analyzed as 'intention to treat', given these patients have the greatest need for timely RIOT. Individuals who underwent multiple liver resections during the study time period were included only once. All patients were treated on an enhanced recovery pathway that included standardized preoperative patient assessment and education, opioid-sparing analgesia, goal-directed fluid therapy, and early postoperative ambulation and oral feeding, as previously published.[3] Standard postoperative follow-up consisted of one visit approximately 1 week after discharge and a second visit approximately 1 month after discharge.

### *Patient-Reported Outcome (PRO) Tool*

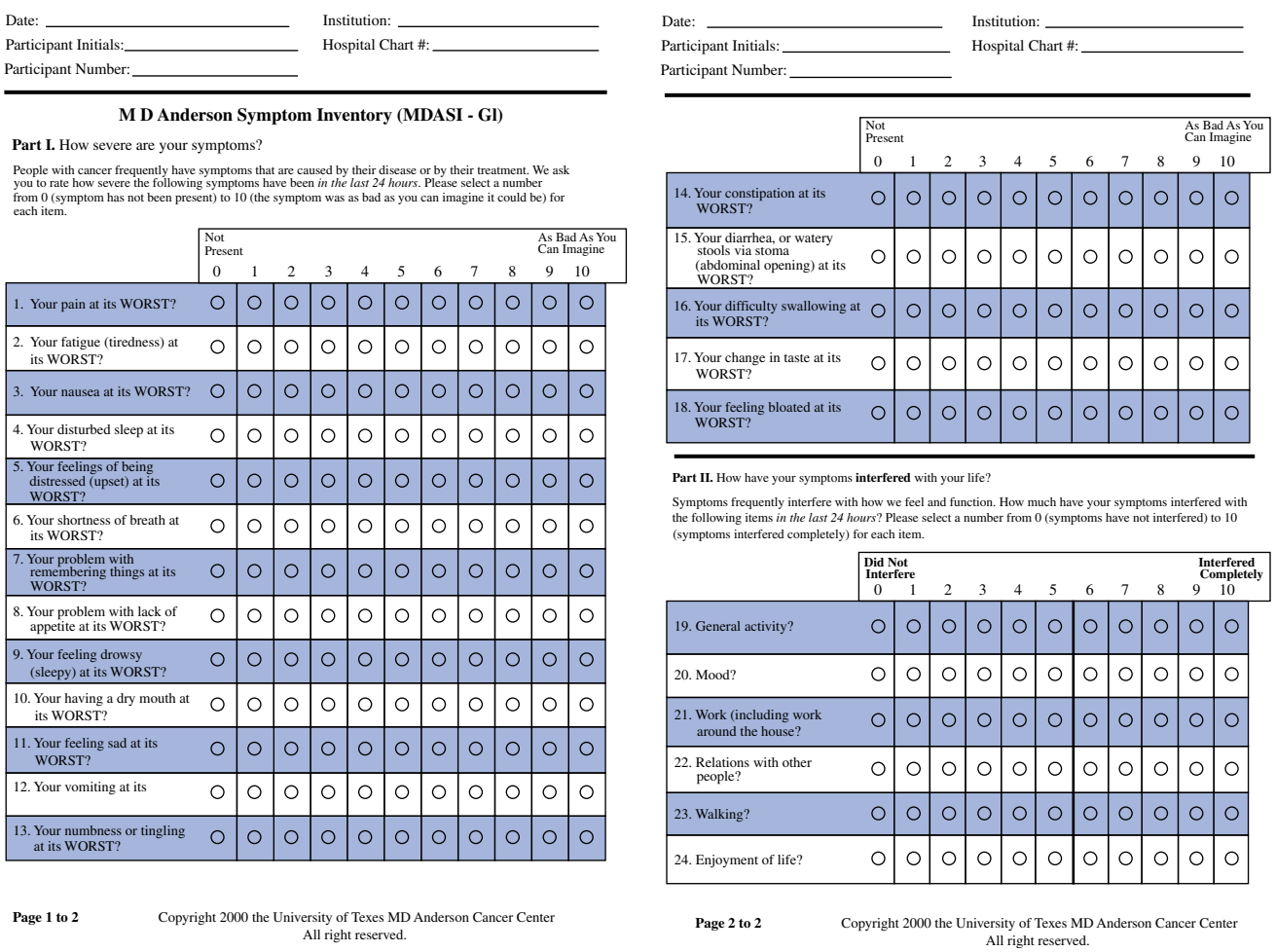
Only patients who completed the MD Anderson Symptom Inventory, Gastrointestinal version (MDASI-GI) (Fig. 1) at their preoperative surgical visit were included in the analysis.[19] This tool is composed of 24 questions, each answered on a numerical scale from 0 to 10. The questionnaire includes a 13-question core symptom assessment, which is common to all versions of the MDASI. The gastrointestinal version (MDASI-GI) contains an additional five questions pertaining to symptoms specific to GI cancers, such as constipation, swallowing, or feeling bloated. The symptom-interference section is comprised of six questions targeting the impact that the patient's symptoms have on daily function and well-being (i.e. life interference). Moderate and severe symptoms were defined as MDASI-GI scores of 4–6/10 and $\geq$7/10, respectively.[20] Moderate and severe symptom burden and life interference were defined as 2–4/10 and $\geq$ 5/10, respectively, per established standards.[21] All patients completed the MDASI-GI within 30 days of their operation.

### *Data Collection and Outcome Measurement*

Basic demographic factors were collected for all patients. Preoperative factors included in this study were performance status based on the Eastern Cooperative Oncology Group (ECOG) grading system,[22] receipt of preoperative chemotherapy, American Society of Anesthesiologists (ASA) classification, known history of previous liver resection, and preoperative laboratory values. Preoperative diagnoses were categorized into primary or secondary malignancies of the liver. It was noted whether the patient was intended for a major liver resection, defined as involving three or more contiguous liver segments,[23] and whether there was a concurrent multivisceral operation to be performed at the same time as the liver resection (most typically, primary colorectal cancer resection). Only factors that could be known at the preoperative surgical visit were included.

Anthropometric analysis was performed on all patients with a preoperative computed tomography (CT) scan within 90 days of surgery. Skeletal muscle area ($cm^2$), subcutaneous adipose area ($cm^2$), and visceral adipose area ($cm^2$) were measured at the L3 level using advanced imaging software (SpliceOmatic, V5.0; TomoVision, Magog, QC, Canada). All areas were standardized to height ($m^2$), and skeletal muscle index (SMI) was expressed in $cm^2/m^2$. SMI was considered to be indicative of sarcopenia at $\leq$ 53 $cm^2/m^2$ for male patients with a BMI $\geq$ 25, $\leq$ 43 $cm^2/m^2$ in male patients with a BMI $<$ 25, and $\leq$ 41 $cm^2/m^2$ for women, independent of BMI as previously published.[24–26] Sarcopenic obesity was defined as the presence of sarcopenia and obesity based on percentage of body fat.[26]

All patients were seen postoperatively by an experienced surgical oncologist and assigned a time of RIOT



Date: _____ Institution: _____
Participant Initials: _____ Hospital Chart #: _____
Participant Number: _____

**M D Anderson Symptom Inventory (MDASI - GI)**

**Part I.** How severe are your symptoms?

People with cancer frequently have symptoms that are caused by their disease or by their treatment. We ask you to rate how severe the following symptoms have been *in the last 24 hours*. Please select a number from 0 (symptom has not been present) to 10 (the symptom was as bad as you can imagine it could be) for each item.

| | Not Present 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | As Bad As You Can Imagine 10 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. Your pain at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 2. Your fatigue (tiredness) at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 3. Your nausea at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 4. Your disturbed sleep at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 5. Your feelings of being distressed (upset) at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 6. Your shortness of breath at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 7. Your problem with remembering things at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 8. Your problem with lack of appetite at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 9. Your feeling drowsy (sleepy) at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 10. Your having a dry mouth at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 11. Your feeling sad at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 12. Your vomiting at its | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 13. Your numbness or tingling at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

Page 1 to 2



Date: _____ Institution: _____
Participant Initials: _____ Hospital Chart #: _____
Participant Number: _____

| | Not Present 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | As Bad As You Can Imagine 10 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 14. Your constipation at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 15. Your diarrhea, or watery stools via stoma (abdominal opening) at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 16. Your difficulty swallowing at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 17. Your change in taste at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 18. Your feeling bloated at its WORST? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

**Part II.** How have your symptoms **interfered** with your life?

Symptoms frequently interfere with how we feel and function. How much have your symptoms interfered with the following items *in the last 24 hours*? Please select a number from 0 (symptoms have not interfered) to 10 (symptoms interfered completely) for each item.

| | Did Not Interfere 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | Interfered Completely 10 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 19. General activity? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20. Mood? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 21. Work (including work around the house? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 22. Relations with other people? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 23. Walking? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 24. Enjoyment of life? | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

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**FIG. 1** MD Anderson Symptom Inventory, Gastrointestinal Version (MDASI-GI)

readiness.[14] This was based on a holistic review of all postoperative information available for the patient via subjective assessments and objective assessments from the electronic health record. RIOT readiness was determined for all patients, even those for whom further oncologic therapy was not indicated or recommended. When dichotomized, patient recovery was classified as early RIOT readiness if they were ready to RIOT at $\leq 28$ postoperative days and delayed RIOT readiness at $> 28$ postoperative days, as previously described.[14]

### *Statistical Analysis*

Categorical variables are expressed as number of patients and percentages and were compared using Pearson's Chi square or Fisher's exact test, as appropriate. Continuous variables are expressed as mean with standard deviation, or median with interquartile range (IQR), and were compared using the Mann–Whitney U test. All $p$ values were two-sided and statistical significance was set at $p < 0.05$. Preoperative patient factors with a $p$ value $< 0.1$ were included in a multivariable analysis using a generalized linear regression model for time to RIOT readiness. Statistical analysis was performed using JMP Pro software version 12 (SAS Institute Inc., Cary, NC, USA).

## RESULTS

### *Study Participants*

A total of 107 patients who underwent oncologic liver resection during the designated time interval completed the preoperative PRO tool and were included in this study, of a total of 133 eligible patients (80%). Demographic and baseline preoperative patient factors are shown in Table 1, parsed by early versus delayed RIOT readiness. The median patient age for the entire cohort was 57 years, with a nearly equal sex distribution. Forty-eight percent of patients were sarcopenic, represented by 39 (53%) of the early RIOT readiness group and 9 (33%) of the delayed RIOT readiness group. Twenty-one percent had sarcopenic

**TABLE 1** Baseline patient factors ($n$ = 107)

| Factor | Early RIOT readiness (≤ 4 weeks) ($n$ = 79) | Delayed RIOT readiness (> 4 weeks) ($n$ = 28) | $p$ value |
|---|---|---|---|
| Age, years [median (IQR)] | 56 (49–62) | 61 (50–67) | 0.120 |
| Sex, female | 44 (56) | 11 (39) | 0.136 |
| Race | | | 0.525 |
| Asian | 2 (3) | 2 (7) | |
| Black or African American | 4 (5) | 3 (11) | |
| White or Caucasian | 64 (81) | 21 (75) | |
| Other | 7 (9) | 2 (7) | |
| Unknown | 2 (3) | 0 (0) | |
| BMI, kg/m$^2$ [median (IQR)] | 27.7 (24.1–31.5) | 27.8 (25.1–31.9) | 0.918 |
| Sarcopenia[a] | 39 (53) | 9 (33) | 0.074 |
| Sarcopenic obesity[a] | 16 (22) | 5 (19) | 0.789 |
| ECOG performance status | | | 0.802 |
| 0 | 34 (43) | 10 (36) | |
| 1 | 42 (55) | 18 (64) | |
| 2 | 1 (1) | 0 (0) | |
| 3 | 2 (3) | 0 (0) | |
| ASA grade III | 104 (97) | 29 (100) | 0.565 |
| Preoperative chemotherapy (within 3 months of operation) | 43 (54) | 14 (50) | 0.686 |
| Albumin, gm/dL[a] [median (IQR)] | 4.2 (4.1–4.5) | 4.2 (4.0–4.5) | 0.377 |
| History of previous hepatectomy | 12 (15) | 3 (11) | 0.754 |
| Primary malignancy of the liver | 22 (28) | 13 (46) | 0.072 |
| Planned major hepatectomy | 15 (19) | 13 (46) | 0.005 |
| Planned multivisceral resection | 7 (9) | 7 (25) | 0.030 |

Data are expressed as $n$ (%) unless otherwise stated

*RIOT* return to intended oncologic therapy, *IQR* interquartile range, *BMI* body mass index, *ASA* American Society of Anesthesiologists, *ECOG* Eastern Cooperative Oncology Group

[a]Missing data: sarcopenia metrics available for 100/107 (93%) patients; albumin metrics available for 106/107 (99%) patients

obesity. Among all patients, 57 had received preoperative chemotherapy (54% early vs. 50% delayed group) and 15 patients had a history of previous liver resection (15% early vs. 11% delayed group). There were more patients planned for a major hepatectomy in the delayed group compared with the early RIOT readiness group (46% vs. 19%; $p$ = 0.005) and more patients were scheduled for a concurrent multivisceral resection in the delayed group compared with the early group (25% vs. 9%; $p$ = 0.030). The most common diagnosis was metastatic colorectal cancer (54 patients [50%]).

### *Baseline Symptom Burden*

On preoperative symptom assessment with the MDASI-GI, 56 patients (52%) reported at least one moderate symptom score and 22 (21%) reported at least one severe score. Fifty-three patients (50%) reported moderate life interference and 30 patients (28%) reported severe life interference. Preoperative symptom and life interference scores are detailed in Table 2. Core symptom items with the highest average score were fatigue (mean 1.93 ± 2.23), disturbed sleep (mean 1.8 ± 2.42), and distress (1.70 ± 2.18). The GI section had lower scores altogether, with constipation (mean 0.87 ± 2.00), diarrhea or watery stools via stoma (mean 0.79 ± 1.92), and feeling bloated (0.67 ± 1.61) having the highest ratings. The symptom with the highest number of severe ratings was disturbed sleep (7%), with 21% of patients having a moderate or greater rating for this item. Twenty-one percent of patients also reported moderate/severe fatigue and 15% reported moderate/severe numbness or tingling. In regard to life interference, symptoms interfered most significantly with general activity (1.77 ± 2.75), work (1.75 ± 2.54), and mood (1.66 ± 2.19). Inability to work had the highest

**TABLE 2** Symptoms and symptom-life interference ($n$ = 107)

| | Mean (± SD) | Median (IQR) | Moderate[a,b] [$n$ (%)] | Severe[a,b] [$n$ (%)] |
|---|---|---|---|---|
| Core symptom items[a] | | | | |
| Pain | 1.04 ± 1.87 | 0 (0–1) | 12 (11) | 2 (2) |
| Fatigue (tiredness) | **1.93 ± 2.23** | 1 (0–3) | 19 (18) | 4 (4) |
| Nausea | 0.41 ± 1.24 | 0 (0–0) | 5 (5) | 1 (1) |
| Disturbed sleep | **1.80 ± 2.42** | 0 (0–3) | 17 (16) | 7 (7) |
| Distress (upset) | **1.70 ± 2.18** | 1 (0–3) | 13 (12) | 5 (5) |
| Shortness of breath | 0.41 ± 1.09 | 0 (0–0) | 2 (2) | 0 (0) |
| Remembering things | 1.05 ± 1.68 | 0 (0–2) | 3 (3) | 3 (3) |
| Lack of appetite | 0.61 ± 1.70 | 0 (0–0) | 4 (4) | 3 (3) |
| Drowsy | 1.26 ± 1.80 | 0 (0–2) | 15 (14) | 0 (0) |
| Dry mouth | 0.84 ± 1.69 | 0 (0–1) | 6 (6) | 3 (3) |
| Sad | 0.97 ± 1.82 | 0 (0–1) | 10 (9) | 1 (1) |
| Vomiting | 0.06 ± 0.41 | 0 (0–0) | 1 (1) | 0 |
| Numbness or tingling | 1.38 ± 2.21 | 0 (0–2) | 12 (11) | 5 (5) |
| GI symptom items[a] | | | | |
| Constipation | **0.87 ± 2.00** | 0 (0–1) | 5 (5) | 4 (4) |
| Diarrhea, watery stools | **0.79 ± 1.92** | 0 (0–0.25) | 5 (5) | 4 (4) |
| Difficulty swallowing | 0.07 ± 0.38 | 0 (0–0) | 0 (0) | 0 (0) |
| Change in taste | 0.46 ± 1.62 | 0 (0–0) | 1 (1) | 4 (4) |
| Feeling bloated | **0.67 ± 1.61** | 0 (0–0) | 6 (6) | 2 (2) |
| Life interference[b] | | | | |
| General activity | **1.77 ± 2.75** | 0 (0–3) | 18 (17) | 17 (16) |
| Mood | **1.66 ± 2.19** | 1 (0–3) | 31 (29) | 14 (13) |
| Work | **1.75 ± 2.54** | 0 (0–3) | 20 (19) | 18 (17) |
| Relations with other people | 0.64 ± 1.55 | 0 (0–0) | 10 (9) | 5 (5) |
| Walking | 0.68 ± 1.65 | 0 (0–0) | 15 (14) | 4 (4) |
| Enjoyment of life | 1.45 ± 2.43 | 0 (0–2) | 20 (19) | 13 (12) |

The highest three scores for each section are indicated in bold

*SD* standard deviation, *IQR* interquartile range, *GI* gastrointestinal

[a]Moderate symptom: score of 4–6 on any item; severe: score of ≥ 7 on any item

[b]Moderate interference: score of 2–4/10 on any item; severe: score of ≥ 5 on any item

number of severe ratings (17%), with 34% of patients having moderate/severe interference for this item.

### *The Impact of Symptom Burden on Return to Intended Oncologic Therapy (RIOT) Readiness*

The median time to RIOT readiness for patients with a severe preoperative symptom burden was 35 days (IQR 28–42), compared with 21 days (IQR 21–28) for those without a severe symptom burden ($p < 0.001$) (Fig. 2). A full comparison of baseline factors for those with and without severe preoperative symptoms is available as electronic supplementary Table 1. The median time to RIOT readiness was 28 days for patients both with and without severe preoperative life interference (IQR 21–42 vs. IQR 21–28; $p = 0.140$). Using a generalized linear regression model, severe preoperative symptom burden was determined to be independently predictive of longer time to RIOT readiness, adding an average of 7.5 days (95% confidence interval [CI] 2.6–12.3) to RIOT readiness time ($p = 0.002$). Severe preoperative life interference was not associated with RIOT readiness time. Other factors available preoperatively that impacted RIOT readiness included having a primary liver cancer (estimate 4.3, 95% CI 0.1–8.4; $p = 0.043$), planned major hepatectomy (estimate 7.9, 95% CI 3.7–12.1; $p < 0.001$), and planned multivisceral resection (estimate 9.0, 95% CI 3.4–14.6; $p = 0.002$). These data are shown in Table 3.

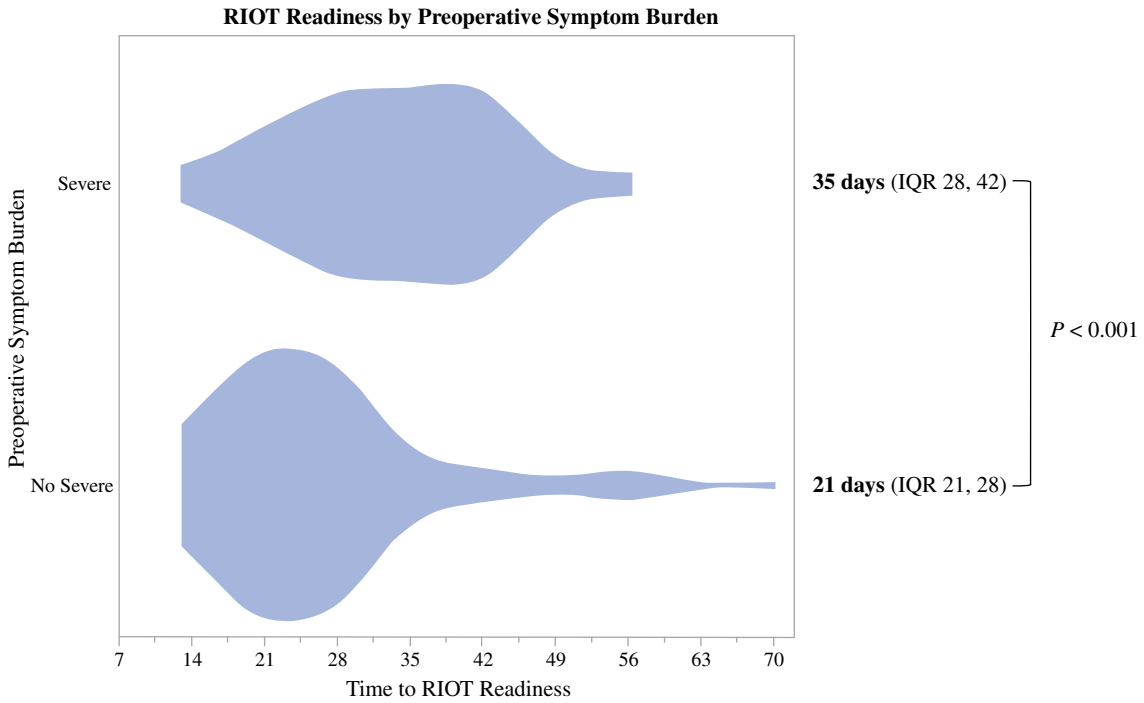


**FIG. 2** Time to RIOT readiness based on preoperative symptom burden, *RIOT* return to intended oncologic therapy, *IQR* interquartile range

**TABLE 3** Preoperative factors associated with RIOT readiness

| Factor | *N* (%) | Median RIOT readiness score (IQR) | Univariable *p* value | Estimate (95% CI) | Multivariable *p* value |
|---|---|---|---|---|---|
| Age > 65 years | 26 (24) | 28 (21–42) | 0.251 | | |
| ECOG ≥ 1 | 51 (48) | 28 (21–35) | 0.346 | | |
| Sarcopenia[a] | 48 (48) | 21 (20–28) | 0.030 | − 2.2 (− 5.9 to 1.6) | 0.253 |
| Preoperative chemotherapy | 57 (53) | 28 (21–30) | 0.947 | | |
| Severe symptom burden[b] | 22 (21) | 35 (28–42) | 0.006 | 7.5 (2.6–12.3) | **0.002** |
| Severe symptom-life interference[c] | 30 (28) | 28 (21–42) | 0.428 | | |
| Primary liver cancer | 35 (33) | 28 (21–42) | 0.041 | 4.3 (0.1–8.4) | **0.043** |
| Planned major hepatectomy | 27 (25) | 28 (28–42) | < 0.001 | 7.9 (3.7–12.1) | < **0.001** |
| Planned multivisceral resection | 14 (13) | 32 (21–46) | 0.007 | 9.0 (3.4–14.6) | **0.002** |

Factors with $p < 0.05$ are indicated in bold

*RIOT* return to intended oncologic therapy, *ECOG* Eastern Cooperative Oncology Group, *CI* confidence interval, *IQR* interquartile range, *GI* gastrointestinal

[a]Missing data: sarcopenia metrics available for 100/107 (93%) patients

[b]Severe symptom burden = any core/GI symptom score ≥ 7/10

[c]Severe interference: score of ≥ 5 on any interference item

## DISCUSSION

Based on this analysis, patients who reported severe preoperative symptoms before liver resection had a longer time to RIOT readiness. The mechanism behind this association is likely delayed postoperative recovery. Certainly, if delayed recovery delays or prevents RIOT, it can translate to worse cancer-specific survivals as patients are forced to postpone necessary systemic or local therapies.[1] Importantly, this finding remained statistically significant after controlling for other traditionally relevant factors that are known at the time of the preoperative visit.

On multivariable analysis, other preoperative factors that are commonly used for risk assessment, including age, ECOG performance status, use of preoperative chemotherapy, and sarcopenia, were not found to be

associated with RIOT readiness. Preoperative ECOG performance status, almost universally used for the functional assessment of cancer patients, was not associated with postoperative time to RIOT readiness. Data regarding sarcopenia in similar patient cohorts are variable, with some studies suggesting that sarcopenia is associated with higher rates of postoperative complications[7,9,10] and survival rates,[7] and others finding no significant relationship between sarcopenia and outcomes.[11] In this study, univariable analysis found that sarcopenia was associated with shorter time to RIOT readiness, although this association did not remain statistically significant after controlling for other factors. Aside from severe preoperative symptoms, the only other preoperative factors found to prolong RIOT readiness were known primary liver malignancy, planned major hepatectomy, and planned multivisceral resection. These factors are largely non-modifiable. Thus, the granular data provided directly from the patient regarding their own preoperative status may be the only modifiable risk factor.

It is important to note the magnitude of preoperative symptom burden in patients undergoing hepatectomy for malignancy. The majority of patients rated at least one symptom as moderate and 21% had at least one severe preoperative symptom. While symptom-life interference was not significantly associated with RIOT readiness, 50% of patients reported moderate interference and 28% had severe interference. Among the 18 symptom items, fatigue, disturbed sleep, and distress had the highest ratings and were most commonly rated as severe. These data are useful for providers to know which specific symptoms to look for, and which may serve as potential targets for preoperative interventions in order to hasten postoperative recovery. While a number of studies have used PROs to describe quality of life and recovery after liver resection,[27–30] very few have demonstrated the prognostic value of PROs in patients undergoing oncologic liver resection.[12] Data from the present study demonstrate the relationship between symptom burden and RIOT readiness, and, given the literature supporting the impact of PROs on cancer-specific survival outcomes,[15–17] this combined information leads to a conclusion that there is likely a long-term benefit to identifying and targeting severe symptoms preoperatively.

Limitations to this study include its retrospective nature and possible selection bias. Patients excluded due to non-completion of the PRO tool were random, as it is the intention of our research group to capture all patients. Furthermore, data from our previously published work in this domain show no difference in RIOT readiness times between those who did and did not complete preoperative MDASI-GI surveys.[14] There is also the potential for confounding by perioperative and surgical factors, such as complications, given their impact on RIOT readiness.[14] The hypothesis of the present study was to evaluate the relationship between preoperative PROs and RIOT readiness, and thus it included only factors known preoperatively in order to inform future risk assessment for patients being scheduled for elective oncologic liver surgery.

## CONCLUSIONS

Patient-reported symptom burden is an underutilized resource for preoperative risk assessment. The data presented here suggest that patients who report severe symptoms preoperatively have delayed surgeon-determined clearance to return to necessary oncologic therapy. Additionally, other traditionally assessed factors, such as age, performance status, and even sarcopenia, were not predictive of RIOT readiness. Patients undergoing liver resection for malignancy often require adjuvant therapy, and delays in initiation may translate to poor long-term outcomes. Therefore, efforts to identify and remediate preoperative symptoms may improve patient recovery and ultimately survival.

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