#### **ORIGINAL ARTICLE**



## The liver transplant surgeon Mondays blues: an Italian perspective

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#### **Abstract**

Poor data exist on the influence of holidays and weekdays on the number and the results of liver transplantation (LT) in Italy. The study's main objective is to investigate the impact of holidays and the different days of the week on the LT number and early graft survival rates in a multi-centric Italian series. We performed a retrospective analysis on 1,026 adult patients undergoing first deceased-donor transplantation between January 2004 and December 2018 in the three university centers in Rome. During the 4,504 workdays, 881 LTs were performed (85.9%; one every 5.1 days on average). On the opposite, 145 LTs were done during the 975 holidays (14.1%; one every 7.1 days on average). Fewer LTs were performed on holidays (P = 0.004). There were no substantial differences in donor-, recipient- and transplant-related characteristics in LTs performed on weekdays or holidays. On Monday, fewer transplants were performed (vs. other weekdays: P < 0.0001; vs. Sunday: P = 0.03). At multivariable Cox regression analysis, LTs performed during the holiday or during the different days of the week were not found to be independent risk factors for the risk of 3- and 12-month graft loss. At three-month survival curves, no differences were observed among the transplants performed during the holidays versus the workdays (86.2 vs. 85.0%; P = 0.000). The range of graft survival rates based on the day of the week was 81.6–86.9%, without showing any significant differences (P = 0.57). Fewer transplants are performed on holidays and Mondays. Survivals are not affected by holidays or the day the transplant is performed.

Keywords Liver transplantation · Weekend effect · Graft survival · Deceased donor · Organ shortage

#### **Abbreviations**

CI Confidence intervals
CIT Cold ischemic time

DDLT Deceased-donation liver transplantation

HCC Hepatocellular carcinoma

HR Hazard ratios

HT Holidays transplantation ICU Intensive care unit IQR Interquartile ranges

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LDLT Living-donor liver transplantation

LT Liver transplantation
WDT Workdays transplantation

## Introduction

Liver transplantation (LT) represents the best curative treatment for end-stage liver disease and unresectable hepatocellular carcinoma (HCC), with 5-year survival rates ranging 70–80% [1, 2]. Unfortunately, the donor shortage impairs the possibility of completely satisfying the number of LT candidates [3]. Living-donor liver transplantation (LDLT) represents an attractive solution to this problem, but its use is limited in Western countries mainly due to the risks of live donor morbidity [4, 5]. Therefore, deceased-donation LT (DDLT) still represents the primary resource for liver graft procurement. However, also DDLT requires sponsoring, motivation, education, training, and adequate funding to increase organ donation and allocation [6].



Transplant surgery is a non-elective surgical procedure with unpredictable surgical timing determined by the availability of donor organs and the need to optimize the graft cold ischemic time (CIT) [7, 8]. Consequently, transplant surgery is often performed at night or during the weekends.

Studies focused on other types of emergency surgery reported higher mortality rates in patients admitted during the night or on the weekends, mainly due to limited human resources, sleep deprivation, and surgery delaying for timesensitive interventions [9–13].

In transplant surgery, postponing the donation procedure to start during regular working hours relates to several potential drawbacks, like the inappropriate use of the intensive care unit (ICU) beds, the risk of losing the donor due to hemodynamic instability, and the interference with elective scheduled surgery in the donor and recipient hospitals [7, 8, 14].

Some studies have already investigated the effect of night shifts and weekends on LT results [15–19], showing similar post-LT survivals [20–22]. However, a potential selection bias caused by an increased rate of organ discharge during the weekend could mask a negative post-operative effect, mainly if marginal donors are more commonly declined [21, 23, 24].

The study aims to investigate the effect of holidays and weekends on the transplantation activity in three university transplant centers in Rome to establish if an "outside working hours" effect should be reported in terms of the number of LT performed and post-LT outcomes.

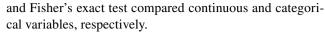
## **Materials and methods**

We performed a retrospective analysis of the data from 1,026 adult (≥ 18 years) patients undergoing a first DDLT between January 1, 2004, and December 31, 2018, in the three University Centers of Rome (Sapienza University, Tor Vergata University, and Cattolica University).

The day of LT operation starting was coded as the day of the operation. We defined Holidays Transplantation (HT) as any LT operation that occurred: (a) between 20:00 h on a Saturday and 08:00 h on a Monday; and (b) during one of the thirteen different Italian public holidays. Work days transplantation (WDT) was defined as any transplant performed during regular working days (from Monday morning to Saturday evening).

## Statistical analysis

Continuous variables were reported as medians and interquartile ranges (IQR). Categorical variables were reported as numbers and percentages. The Mann–Whitney U test



A multivariable Cox regression analysis was constructed to identify the risk factors for 3 and 12-month graft loss. Hazard ratios (HR) and 95.0% confidence intervals (95% CI) were reported.

Survival probabilities were estimated using the Kaplan–Meier method. Survival rates comparisons were estimated using the log-rank method. Variables with a P < 0.05 were considered statistically significant. We used the SPSS statistical package version 24.0 (SPSS Inc., Chicago, IL, USA).

## **Results**

The donor-, recipient-, and LT procedure-related characteristics are reported in Table 1. During the study period, 4504 workdays and 975 public holidays were calculated. A total number of 881/1026 (85.9%) WDTs were performed, with an average of one transplant every 5.1 days). A total of 145/1,026 (14.1%) HT were done, with an average of one every 7.1 days. Overall, fewer LTs were performed during the holidays (P = 0.004).

As for the recipient characteristics, no statistically relevant differences were observed between the two groups. In detail, the recipients transplanted during the workdays presented similar age (median: 56 vs. 56 years; P = 0.2), MELD score (median: 16 vs. 18; P = 0.1), HCC (36.1 vs. 41.4%; P = 0.2), and underlying liver disease.

As for the donors, several similarities were observed between the two groups. In detail, the WDT group presented a similar sharing (regional share: 54.3 vs. 55.9%; P = 0.8), age (median: 54 vs. 50 years; P = 0.5), causes of death, comorbidities, smoking or alcohol abuse history, hemodynamic instability (26.3 vs. 29.7%; P = 0.4), and blood tests of liver function respect to the HT group. The only statistically relevant difference was a higher number of biopsies performed during the workdays (46.2 vs. 37.2; P = 0.048).

As for the transplant procedure, CIT was shorter during the holidays (median: 410 vs. 420 min; P = 0.02). Also, the BAR score was statistically significant (P = 0.008). Other donor-specific scores like the DRI, the Eurotransplant-DRI, and the D-MELD were not statistically relevant.

After LT, reoperation rates were similar in the two groups (11.8 vs. 10.3%; P=0.7). As for the early survival rates after LT, 3-month patient death rates were similar between WDT and HT groups (13.5 vs. 13.1%; P=1.0). Similar results were observed in terms of 3-month graft loss (15.0 vs. 13.8%; P=0.8) and need for early re-transplantations (1.1 vs. 0.7; P=1.0).

No statistical differences were observed in the survival analysis when the graft survivals were compared in the



Table 1 Recipient, donor, and transplant demographics

Variables	WDT (n = 881) HT (n = 145)				
variables	Median (IQR) or n (%)				
Paginiant					
Recipient Age	56 (48–61)	56 (49–63)	0.2		
MELD	,		0.2		
	16 (12–22)	18 (13–22)			
HCC	318 (36.1)	60 (41.4)	0.2		
HCV	331 (37.6)	49 (33.8)	0.4		
HBV	132 (15.0)	24 (16.6)	0.6		
Alcoholic	257 (29.2)	47 (32.4)	0.4		
ALF	49 (5.6)	5 (3.4)	0.4		
NASH	74 (8.4)	15 (10.3)	0.4		
Other	118 (13.4)	20 (13.8)	0.9		
Donor					
Km distance procure- ment	10 (10–303)	10 (10–246)	0.9		
Regional share	478 (54.3)	81 (55.9)	0.8		
Use of airplane	189 (21.5)	32 (22.1)	0.9		
Age	54 (37–67)	50 (36–67)	0.5		
< 40	251 (28.5)	41 (28.3)	1.0		
40–49	124 (14.1)	29 (20.0)	0.08		
50-59	151 (17.1)	20 (13.8)	0.4		
60–69	185 (21.0)	31 (21.4)	0.9		
70–79	132 (15.0)	21 (14.5)	1.0		
≥80	38 (4.3)	3 (2.1)	0.3		
Male gender	478 (54.3)	74 (51.0)	0.5		
Length of ICU stay	3 (2–6)	3 (2–6)	0.1		
Split liver	28 (3.2)	4 (2.8)	1.0		
Race	, ,	, ,			
Caucasian	853 (96.8)	144 (99.3)	0.1		
Latin American	10 (1.1)	0 (-)	0.4		
Black	2 (0.2)	1 (0.7)	0.4		
Arabian	3 (0.3)	0 (-)	1.0		
Asian	13 (1.5)	0 (-)	0.2		
Cause of death	13 (1.3)	0()	0.2		
Trauma	235 (26.7)	41 (28.3)	0.7		
Anoxia		8 (5.5)	0.7		
CVA	37 (4.2) 583 (66.2)	91 (62.8)	0.5		
Other	20 (2.3)	5 (3.4)	0.4		
Weight	72 (65–80)	70 (65–80)	0.3		
Height	170 (161–175)	170 (161–175)	0.7		
BMI	25 (23–28)	25 (23–27)	0.7		
Liver weight kg	1.1 (1.2–1.3)	1.1 (1.2–1.3)	0.4		
Comorbidities	50 (CE)	44 (0.5)			
DM2	59 (6.7)	14 (9.7)	0.2		
Hypertension	301 (34.2)	53 (36.6)	0.6		
Dyslipidemia	66 (7.5)	13 (9.0)	0.5		
Previous surgery	393 (44.6)	62 (42.8)	0.7		
Upper surgery	41 (4.7)	7 (4.8)	0.8		
Smoking	266 (30.2)	48 (33.1)	0.5		
Alcohol abuse	32 (3.6)	7 (4.8)	0.5		
Anticore	97 (11.0)	16 (11.0)	1.0		

Table 1 (continued)

Variables	WDT (n = 881)	HT (n = 145)	P	
	Median (IQR) or			
Hemodynamic instability	232 (26.3)	43 (29.7)	0.4	
Hypotension	183 (20.8)	31 (21.4)	0.9	
Cardiac arrest	88 (10.0)	16 (11.0)	0.7	
Any inotrope use	716 (81.3)	120 (82.8)	0.7	
VAS	10 (3–22)	12 (3–30)	0.4	
Azotemia	30 (18–49)	30 (18–45)	0.6	
Creatinine peak	1.0 (0.7–1.3)	0.9 (0.7-1.3)	0.08	
NA peak	151 (145–158)	151 (145–156)	0.3	
AST peak	39 (26–78)	42 (26–78)	0.9	
ALT peak	32 (19–58)	31 (19–56)	0.7	
Total bilirubin peak	0.7 (0.5-1.1)	0.8 (0.4–1.2)	0.6	
GGT	29 (15–59)	27 (14–59)	0.3	
INR	1.20 (1.08-1.31)	1.21 (1.10-1.36)	0.3	
Platelets	154 (112–209)	169 (128–221)	0.1	
Liver biopsy	407 (46.2)	54 (37.2)	0.048	
Transplant				
CIT	420 (375–480)	410 (353–450)	0.02	
DRI	2.3 (1.8–2.6)	2.3 (1.8–2.6)	0.4	
ETDRI	1.8 (1.5-2.0)	1.8 (1.5-2.0)	0.2	
D-MELD	782 (509–1204)	860 (553–1252)	0.3	
BAR	7 (3–9)	7 (4–10)	0.008	
Reoperation during the LT hospitalization	104 (11.8)	15 (10.3)	0.7	
Patient survival				
30 days	76 (8.6)	12 (8.3)	1.0	
60 days	105 (11.9)	17 (11.7)	1.0	
90 days	119 (13.5)	19 (13.1)	1.0	
Graft survival				
30 days	86 (9.8)	13 (9.0)	0.9	
60 days	118 (13.4)	18 (12.4)	0.9	
90 days	132 (15.0)	20 (13.8)	0.8	
Early re-LT (30 days)	10 (1.1)	1 (0.7)	1.0	

WDT workdays transplantation, HT holidays transplantation, IQR inter-quartile ranges, MELD model for end-stage liver disease, HCC hepatocellular cancer, HCV hepatitis C virus, HBV hepatitis B virus, ALF acute liver failure, NASH non-alcoholic liver disease, ICU intensive care unit, CVA cerebro-vascular accident, BMI body mass index, DM2 diabetes mellitus type 2, VAS vaso-active score, Na sodium, AST aspartate amino-transferase, ALT alanine amino-transferase, GGT gamma-glutamyl transferase, INR international normalized ratio, CIT cold ischemia time, DRI donor risk index, ETDRI Euro-Transplant-donor risk index, D-MELD donor-model for end-stage liver disease, BAR balance of risk, LT liver transplantation

two groups. In detail, 1-, 2-, and 3-month graft survival rates were 91.0 vs. 90.2%, 87.6 vs. 86.7%, and 86.2 vs. 85.0% in the WDT and HT groups, respectively (log-rank P = 0.7) (Fig. 1). Similarly, 12-, 36-, and 60-month graft survival rates were not significantly different, with 82.1 vs.



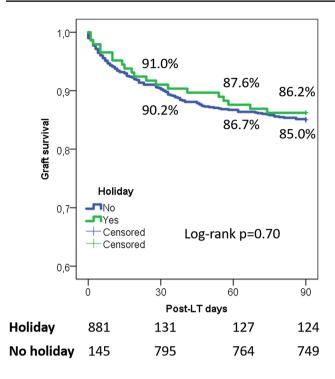


Fig. 1 Survival curves evaluating the graft survival rates in the holidays and in the workdays

**Table 2** Number of transplants according to the days of the week

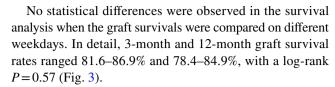
Day	N LTs	%	P
Monday	83	8.1	_
Tuesday	171	16.7	M vs. Tu < 0.0001
Wednesday	159	15.5	M vs. We $< 0.0001$
Thursday	167	16.3	M vs. $Th < 0.0001$
Friday	174	17.0	M vs. Fr < 0.0001
Saturday	160	15.6	M vs. Su < 0.0001
Sunday	112	10.9	M vs. Sa 0.03
Total	1026	100.0	_

N number, LT liver transplantation

80.6%, 76.9 vs. 75.4%, and 71.9 vs. 71.4% survival rates in the WDT and HT groups, respectively.

# Number of LT and outcomes on the different weekdays

In Table 2, the number of transplants performed each week-day was reported. In detail, the number of LT was Monday = 83; Tuesday = 171; Wednesday = 159; Thursday = 167; Friday = 174; Saturday = 160; Sunday = 112. Analyzing the number of transplants performed on different days, Monday always reported fewer transplants (vs. other weekdays: P < 0.0001; vs. Sunday: P = 0.03) (Fig. 2).



## Risk factors for 3- and 12-month graft loss

At multivariable Cox regression analysis, only MELD (HR 1.04, 95.0% CI 1.01–1.06; P = 0.001) and CIT (HR 1.11, 95.0% CI 1.004–1.22; P = 0.04) were independent risk factors for 3-month graft loss. Neither LT performed during the holiday (HR 0.57, 95.0% CI 0.18–1.80; P = 0.34) nor the LT performed during the different days of the week were statistically relevant variables (Table 3).

Similarly, only MELD (HR 1.03, 95.0% CI 1.01–1.05; P=0.001) was an independent risk factor for 12-month graft loss. Neither LT performed during the holiday (HR 0.60, 95.0% CI 0.22–1.63; P=0.31) nor the LT performed during the different days of the week were statistically relevant variables (Table 4).

### Discussion

According to the present multicentre study results, the number of LTs is reduced on holidays and during the Monday. However, no substantial differences in terms of early and late survival rates were observed. Our data are in concordance with several previous studies.

Significant evidence exists on the poor outcomes reported in patients admitted for surgical and clinical emergencies during the weekends [9–13, 25, 26]. Limited resources, poor availability of specialists, and limited access to ICU departments have been evocated as the factors influencing these worse outcomes. This evidence has not been uniquely confirmed in the transplant setting, with discordant survival results observed when the transplants were performed during the nights, the weekends, or the holidays [15–18, 28].

A meta-analysis based on 95,346 LT patients, of whom 32,079 received a LT during the weekend, and 31,333 operated overnights, showed conflicting results in terms of overall survival, with evidence inconclusive for a variety of morbidity outcomes, and with studies demonstrating either a deterioration of outcome, no effect, or an improved outcome for after-hours procedures [29]. For example, one study from the United States reported the risk of early death to be doubled, and the operative time significantly increased when the liver was transplanted overnight [18]. On the opposite, another study from the same country did not observe any effects on mortality, however, documenting a statistically significant decrease in 1-year graft survival for the weekend compared to the workday group [17].



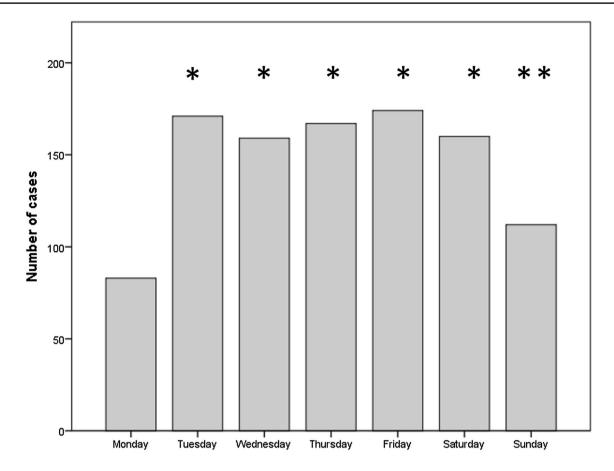


Fig. 2 Distribution of transplantations according to the weekdays. \*P < 0.0001; \*\*P = 0.03

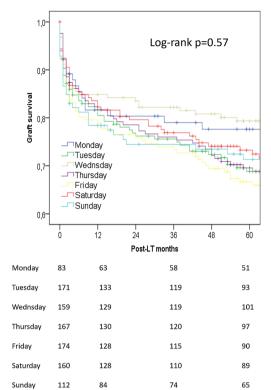
Several explanations have been advocated for explaining such results, like (a) an impaired technical performance or perioperative decision making due to fatigue, (b) several previous surgeries performed by the transplant team on call for the weekend, (c) and the surgical services support staff heterogeneously composed by members of cross-disciplinary teams also involved in other surgical emergencies.

The adverse effects of fatigue on technical and cognitive skills are well-documented for surgeons and anaesthesiologists [9, 10]. Nevertheless, fatigue is only one of the factors jeopardizing surgical performance during after-hours and holidays. Poor post-operative outcomes for out-hours procedures have also been attributed to care transitions, with a lack of availability of specialists, less familiarity with the procedure, greater dependence on residents, and unbefitting staffing. Several subspecialties have dealt with these pitfalls by providing specialized protocol and team on call, guaranteeing the same standard of care and procedural outcome independently from the hour and day. This issue is particularly real for many transplant centers, which could explain why an adverse effect of out-of-hours transplant outcome has not been clearly demonstrated.

Interestingly, the results of our series are in line with these results, with similar 3- and 12-month graft survival rates in patients transplanted during holidays vs. workdays or on the different weekdays, comprehending the weekend days. Such a result should be explained because the dedicated transplant surgical teams of the centers involved in the study are on call only for the transplant procedures and not involved in other types of surgical emergencies during holidays and nights. Moreover, no changes in the surgical teams that performed the operations on weekdays or holidays were present, with the same equips performing the procedures no matter on the day of the week.

As for the reduction of LT during the holidays, our experience is in line with previous studies. The increase in organ discard rates has been advocated as a potential explanation of this phenomenon during off-days, even after adjustment for organ quality. Carpenter et al. report that liver graft nonusage was 11% higher on the weekend than on weekdays [24]. Mohan et al. reported in a retrospective cohort study based on 181,799 deceased-donor kidneys that kidney discards during the weekend were of a significantly higher quality than weekday discards (kidney donor profile index: 76.5 vs. 77.3%) [21].





Day	3-mo graft survival %
Monday	86.7
Tuesday	85.4
Wednsday	85.5
Thursday	86.2
Friday	81.6
Saturday	86.9
Sunday	84.8

Day	12-mo graft survival %
Monday	81.6
Tuesday	81.7
Wednsday	84.9
Thursday	81.7
Friday	79.0
Saturday	83.6
Sunday	78.4

Day	Log-rank p
Su vs. Mo	0.40
Su vs. Tu	0.72
Su vs. We	0.80
Su vs. Th	0.60
Su vs. Fr	0.32
Su vs. Sa	0.99

Fig. 3 Survival curves evaluating the graft survival rates in the different weekdays

**Table 3** Risk factors for 3-month graft survival

Variables	Beta	SE	Wald	HR	95.0% CI		P
					Lower	Upper	
MELD	0.03	0.01	10.23	1.04	1.01	1.06	0.001
CIT (per hour)	0.10	0.049	4.18	1.11	1.004	1.22	0.04
ALF	0.41	0.34	1.39	1.50	0.76	2.95	0.24
Holiday as day of LT	-0.56	0.59	0.92	0.57	0.18	1.80	0.34
Donor age (per year)	0.004	0.005	0.76	1.004	0.99	1.02	0.38
Donor DM2	0.22	0.30	0.52	1.24	0.69	2.23	0.47
HCV	0.10	0.20	0.26	1.11	0.75	1.62	0.61
Recipient age (per year)	0.003	0.008	0.17	1.003	0.99	1.02	0.68
HBV	-0.11	0.27	0.16	0.90	0.53	1.52	0.69
Alcohol	0.07	0.20	0.13	1.07	0.73	1.58	0.72
Donor hemodinamic instability	-0.03	0.19	0.03	0.97	0.67	1.40	0.87
CVA as cause of donor death	0.008	0.20	0.001	1.008	0.69	1.48	0.97
Day of LT							
Sunday	Ref	_	_	1.00	_	_	_
Monday	-0.75	0.69	1.19	0.47	0.12	1.82	0.28
Tuesday	-0.61	0.66	0.86	0.54	0.15	1.97	0.35
Wednesday	-0.62	0.66	0.88	0.54	0.15	1.97	0.35
Thursday	-0.68	0.65	1.07	0.51	0.14	1.83	0.30
Friday	- 0.39	0.65	0.36	0.68	0.19	2.42	0.55
Saturday	-0.74	0.66	1.25	0.48	0.13	1.75	0.26

SE standard error, HR hazard ratio, 95.0% CI 95.0% confidence intervals, MELD model for end-stage liver disease, CIT cold ischemia time, ALF acute liver failure, LT liver transplantation, DM2 diabetes mellitus type 2, HCV hepatitis C virus, HBV hepatitis B virus, CVA cerebro-vascular accident



**Table 4** Risk factors for 12-month graft survival

Variables	Beta	SE	Wald	HR	95.0% CI		P
					Lower	Upper	
MELD	0.03	0.01	10.77	1.03	1.01	1.05	0.001
ALF	0.54	0.31	3.02	1.71	0.93	3.14	0.08
Donor age (per year)	0.005	0.005	1.42	1.01	0.996	1.02	0.23
Holiday as day of LT	-0.51	0.51	1.01	0.60	0.22	1.63	0.31
Recipient age (per year)	0.007	0.007	0.98	1.01	0.99	1.02	0.32
HBV	-0.20	0.25	0.67	0.82	0.50	1.33	0.41
CVA as cause of donor death	0.14	0.18	0.63	1.15	0.81	1.64	0.43
HCV	0.12	0.18	0.50	1.13	0.80	1.60	0.48
Donor hemodynamic instability	0.08	0.17	0.23	1.08	0.78	1.50	0.63
Alcohol	0.04	0.18	0.05	1.04	0.73	1.47	0.83
Donor DM2	-0.06	0.30	0.04	0.94	0.53	1.68	0.84
Day of LT							
Sunday	Ref	_	_	1.00	_	_	_
Monday	0.10	0.31	0.10	1.10	0.60	2.04	0.75
Tuesday	-0.17	0.33	0.27	0.84	0.44	1.61	0.61
Wednesday	-0.003	0.32	0.00	0.997	0.53	1.86	0.99
Thursday	0.14	0.31	0.21	1.15	0.63	2.12	0.65
Friday	-0.02	0.32	0.003	0.98	0.52	1.85	0.95
Saturday	0.76	0.59	1.64	2.14	0.67	6.83	0.20
CIT (per hour)	0.06	0.04	1.96	1.06	0.98	1.16	0.16

SE standard error, HR hazard ratio, 95.0% CI 95.0% confidence intervals, MELD model for end-stage liver disease, CIT cold ischemia time, ALF acute liver failure, LT liver transplantation, DM2 diabetes mellitus type 2, HCV hepatitis C virus, HBV hepatitis B virus, CVA cerebro-vascular accident

Unfortunately, due to the retrospective nature of our study, we were not able to investigate the discard rates during the holidays. However, we noted that a comparable rate of marginal grafts was used during the workdays and holidays (23.6 vs. 27.2%, respectively), therefore suggesting that the reduction in the number of transplants was not only attributable to an increased organ discard, but it probably represents a combination of phenomena also comprehending the reduction in the number of donor procurements caused by the extra-day off before the holiday.

Another concern observed in our series was the evident decline of transplants performed on Mondays, even when compared with the procedures performed on Sundays. This phenomenon, already observed in other geographical areas, has been defined as the "transplant Monday blues" [30]. A straightforward explanation for this phenomenon is the reduction of organ procurements performed on Sunday, eventually decreasing transplant surgery during the following day.

Organ donation requires respect for strict protocols involving many specialists and hospital services, representing a resource- and time-consuming procedure. Hence, postponing the beginning of the donation process on Monday, during which the health care hospital system does not suffer from limited resources, can be considered an alternative

option. Moreover, it must be considered that donors are frequently from hospitals bereft of required specialists (i.e., neurologist or electrophysiologist) that must be called from other district hospitals and are at the same time on call for the emergencies service of their specific specialties. Lastly, another issue explaining the decrease of donations during the weekend is the higher mortality observed during these days in emergency patients admitted for stroke, heat acute disease, and trauma, consequently reducing the available donor pool [11, 13, 31–33]. Unfortunately, solving the problem of the donation decline during the Sunday is not easy, requiring the improvement of clinical services, incentives and resources at the level of donation hospitals. Local, regional and national institutions involved in organ donation promoting should consider these aspects with the intent to implement them. The purpose of the present analysis is to inform the national transplant community where there is potential for an increase in the number of liver grafts for transplantation.

This is the first study reporting an Italian series on this topic. Although the analysis is limited only to the surgical activity of the transplant centers of the Universities of Rome, in the authors' opinion, the results may be representative of the impact of holidays on liver procurement and transplantation in the Italian setting. The study presents some limits. First, the



study is retrospective and multi-centric. Second, no data have been collected on the number of potential donors and the rate and reasons for graft discard on different weekdays or during the holidays.

In conclusion, LT procedures reduce their numbers during the holidays and on Mondays. The results are similar no matter the day the transplant is performed. An improvement of the resources should be applied during the weekends and holidays to improve the number of available organs to reduce the critical gap between the request for transplantation and the pool of available organs. Further studies investigating the impact of the different weekdays on the discard rate are indeed required.

**Author contributions** QL contributed to conception and design of the study; GM, TMM, AWA, RA, GS, and QL contributed to acquisition of data; QL analyzed and interpreted the data; SQ and QL drafted the article; all the authors critically revised the manuscript; and all authors approved the final version.

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## **Declarations**

**Conflict of interest** The authors have no conflict of interest to declare.

**Ethical approval** This is a retrospective study which has been conducted in accordance with the ethical standards as laid in the 1964 Helsinki Declaration.

Research involving human participants and/or animals A study-specific approval was obtained by the local ethical committee of Sapienza University of Rome, AOU Policlinico Umberto I of Rome (leading center of the study).

**Informed consent** The authors obtained an informed consent at the time of transplantation from all the participants of the study for the treatment of their clinical data.

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## References

 Adam R, Karam V, Cailliez V et al (2018) 2018 annual report of the European liver transplant registry (ELTR)-50-year evolution of liver transplantation. Transpl Int 31:1293–1317

- Firl DJ, Sasaki K, Agopian VG et al (2020) Charting the path forward for risk prediction in liver transplant for hepatocellular carcinoma: international validation of HALTHCC among 4089 patients. Hepatology 71:569–582
- 3. Goldberg DS (2016) Defining disparities in liver transplantation: the devil is in the details, Liver Transpl 22:1720–1723
- Lai Q, Sapisochin G, Gorgen A et al (2021) Evaluation of the Intention-to-Treat Benefit of Living Donation in Patients With Hepatocellular Carcinoma Awaiting a Liver Transplant. JAMA Surg 156:e213112
- Pinheiro RS, Waisberg DR, Nacif LS et al (2017) Living donor liver transplantation for hepatocellular cancer: an (almost) exclusive Eastern procedure? Transl Gastroenterol Hepatol 2:68
- Rela M, Rammohan A (2021) Why are there so many liver transplants from living donors in Asia and so few in Europe and the US? J Hepatol 75:975–980
- Ghinolfi D, Lai Q, Pezzati D et al (2018) Use of elderly donors in liver transplantation: a paired-match analysis at a single center. Ann Surg 268:325–331
- 8. Pan ET, Yoeli D, Galvan NTN et al (2018) Cold ischemia time is an important risk factor for post-liver transplant prolonged length of stay. Liver Transpl 24:762–768
- van Zaane B, van KleiWA BWF, Bauer P, Boerma EC, Hoeft A et al (2015) Nonelective surgery at night and in-hospital mortality. Eur J Anaesthesiol 32:477–485
- Gaba D, Howard S (2002) Fatigue among clinicians and the safety of patients. N Engl J Med 347:1249–1255
- Glaser R, Naidu SS, Selzer F, Jacobs AK, Laskey WK, Srinivas VS et al (2008) Factors associated with poorer prognosis for patients undergoing primary percutaneous coronary intervention during off-hours. JACC Cardiovasc Interv 1:681–688
- Freemantle N, Ray D, McNulty D et al (2015) Increased mortality associated with weekend hospital admission: a case for expanded seven day services? BMJ 351:h4596
- Zhou Y, Li W, Herath C et al (2016) Off-hour admission and mortality risk for 28 specific diseases: a systematic review and meta-analysis of 251 cohorts. J Am Heart Assoc 5:e003102
- Hong JC, Busuttil RW (2008) Cold ischemia time and liver graft survival. Am J Transplant 8:481–482
- Anderson BM, Mytton JL, Evison F, Sharif A (2017) Outcomes after weekend admission for deceased donor kidney transplantation: a population cohort study. Transplantation 101:2244–2252
- Baid-Agrawal S, Martus P, Feldman H, Kramer H (2016) Weekend versus weekday transplant surgery and outcomes after kidney transplantation in the USA: a retrospective national database analysis. BMJ Open 6:e010482
- Orman ES, Hayashi PH, Dellon ES, Gerber DA, Barritt IVAS (2012) Impact of nighttime and weekend liver transplants on graft and patient outcomes. Liver Transpl 18:558–565
- Lonze BE, Parsikia A, Feyssa EL et al (2010) Operative start times and complications after liver transplantation. Am J Transplant 10:1842–1849
- Baid-Agrawal S, Martus P, Feldman H et al (2016) Weekend versus weekday transplant surgery and outcomes after kidney transplantation in the USA: a retrospective national database analysis. BMJ Open 6:e010482
- Loss J, Drewitz KP, Schlitt HJ et al (2013) Accept or refuse? Factors influencing the decision-making of transplant surgeons who are offered a pancreas: results of a qualitative study. BMC Surg 13:47
- Mohan S, Foley K, Chiles MC et al (2016) The weekend effect alters the procurement and discard rates of deceased donor kidneys in the United States. Kidney Int 90:157–163
- Gordon Burroughs S, Busuttil RW (2009) Optimal utilization of extended hepatic grafts. Surg Today 39:746–751



- Cavallazzi R, Marik PE, Hirani A et al (2010) Association between time of admission to the ICU and mortality: a systematic review and meta-analysis. Chest 138:68–75
- Carpenter DJ, Chiles MC, Verna EC et al (2019) Deceased brain dead donor liver transplantation and utilization in the United States: nighttime and weekend effects. Transplantation 103:1392–1404
- Crowley RW, Yeoh HK, Stukenborg GJ et al (2009) Influence of weekend hospital admission on short-term mortality after intracerebral hemorrhage. Stroke 40:2387–2392
- Dorn SD, Shah ND, Berg BP, Naessens JM (2010) Effect of weekend hospital admission on gastrointestinal hemorrhage outcomes. Dig Dis Sci 55:1658–1666
- Kostis WJ, Demissie K, Marcella SW et al (2007) Weekend versus weekday admission and mortality from myocardial infarction. N Engl J Med 356:1099–1109
- Halliday N, Martin K, Collett D, Allen E, Thorburn D (2019)
   Is liver transplantation 'out-of-hours' non-inferior to 'in-hours' transplantation? A retrospective analysis of the UK Transplant Registry. BMJ Open 9:e024917
- Hendrikx J, Van Raemdonck D, Pirenne J, Fieuws S, Rex S (2018)
   Outcome of transplantation performed outside the regular working

- hours: a systematic review and meta-analysis of the literature. Transplant Rev 32:168–177
- Chan SC, Dai WC, Lo CM et al (2011) Monday blues of deceaseddonor liver transplantation. Hepatobiliary Pancreat Dis Int 10:26–29
- 31. Albright KC, Raman R, Ernstrom K et al (2009) Can comprehensive stroke centers erase the 'weekend effect'? Cerebrovasc Dis 27:107–113
- Peberdy MA, Ornato JP, Larkin GL et al (2008) Survival from in-hospital cardiac arrest during nights and weekends. JAMA 299:785

  –792
- Laupland KB, Ball CG, Kirkpatrick AW (2009) Hospital mortality among major trauma victims admitted on weekends and evenings: a cohort study. J Trauma Manag Outcomes 3:8

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