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The Impact of Quadriceps Muscle Layer Thickness on Length of Stay of Patients Listed for Renal Transplant

Max Levine [1], Patrick Luke [2], Alp Sener [2], Heather Resvick [3], Stephanie Braga [3], Taralynn St. Kitts [3], Sarah De Marinis [3] and Janet Madill [1,2,*]

[1] Alberta Health Services, Edmonton, AB T3B 0M6, Canada; max.levine@albertahealthservices.ca
[2] London Health Sciences, Renal Transplant Program, London, ON NGA 5A5, Canada; patrick.luke@lhsc.on.ca (P.L.); alp.sener@lhsc.on.ca (A.S.)
[3] School of Food and Nutritional Sciences, Brescia University College, Western University, 1285 Western Road, London, ON N6G 1H2, Canada; hresvick@uwo.ca (H.R.); sbraga@uwo.ca (S.B.); sdemarin@uwo.ca (S.D.M.)
* Correspondence: jmadill7@uwo.ca

Abstract: Background: Quadriceps muscle layer thickness (QMLT), which is measured using ultrasound, is an emerging strategy to identify sarcopenia. Purpose: The purpose of the study was to assess whether pre-operative QMLT values are associated with a prolonged length of stay (LOS; defined as >14 days) following a renal transplant. Methods: Between March 2019 and January 2020, we performed a prospective study among patients undergoing renal transplantation. Physical Frailty scores and QMLT measurements were performed pre-operatively. The primary outcome was a greater LOS following transplant. Secondary outcomes included complications and renal function. *Statistical analysis*: Percentiles divided patients into two categories of QMLT (low and high). Continuous outcomes were compared using a two-sided t-test or Mann–Whitney U test, and Chi-square analysis and Fisher exact testing were used for nominal variables. Results: Of 79 patients, the frailty prevalence was 16%. Among patients with low and higher QMLTs, LOS of >14 days were 21% vs. 3% [$p = 0.04$], respectively. Demographically, there was a higher percentage of patients with living donors in the high- vs. low-QMLT groups (40 vs. 7%). However, in a subgroup analysis excluding living-donor recipients, the difference between groups was preserved (23% vs. 0%, $p = 0.01$). No differences in secondary outcomes were seen between groups. Conclusions: Low quadriceps muscle layer thickness may be associated with a prolonged length of stay for renal recipients. Further research is needed to confirm our findings.

Keywords: kidney transplantation; quadriceps muscle; length of stay; body composition; living donors

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1. Introduction

As of 2019, chronic kidney disease (CKD) was the 10th leading cause of Canadian deaths, with ~4 million Canadians living with this disease [1]. Recent statistics from organ transplants in Canada [2022] indicate that there were 1795 kidney transplants, 2813 wait-listed patients, and 117 patients who died while waiting [2]. Thus, identifying kidney patients with the potential for long-term positive outcomes is vitally important.

Sarcopenia, which is defined as the loss of lean muscle mass and muscle strength, which can lead to frailty, represents an important issue for patients with chronic diseases such as end-stage organ failure [3]. Sarcopenia has been shown to increase morbidity and mortality post-lung and -liver transplantation in two recent meta-analyses [4,5]. The prevalence of frailty is higher in sarcopenic compared to non-sarcopenic patients, even when their age, nutritional status, and systemic inflammatory markers are similar [6]. While they are not interchangeable phenomena, frailty and sarcopenia can stem from common pathophysiologic processes, such as the oxidative stress and/or inflammation seen in patients with chronic kidney disease, as described by Liguori L et al. 2018 [7,8].

Frailty has also emerged as a relevant prognostic tool in the kidney transplant population [9]. There are several frailty scales and measures, such as the Clinical Frailty Scale (CFS) frailty scale and the Short Physical Performance Battery (SPPB), among others, each with its own subjectivity and limitations [10–12]. However, frailty has been assessed in patients with chronic kidney disease using the validated Physical Frailty Phenotype (PFP) metric. This tool has been used in 72% of chronic renal disease studies involving ~36,000 patients, as evidenced by a systematic review [13]. The scoring reflects measures of muscle function, mass, and activity [14]. Using PFP, kidney transplant (KT) patients who were identified as frail were found to have longer lengths of stay (LOS) in hospital after transplants [15]. Haugen et al. reported a prevalence of 13.3% frailty in KTs at an evaluation with 8.2% living-donor KTs and 17.8% deceased-donor KTs at the time of transplantation [16]. In further support of the claim that frail kidney recipients have negative health outcomes, Harhay et al., 2020 conducted a systematic review, examining 641 articles worldwide. This review indicated that frail KT patients were two times more likely to die vs. non-frail ones [17]. Similarly, McAdams-DeMarco et al., 2015 reported that frailty was associated with a higher risk of death, with an HR of 2.17, $p = 0.047$, in a prospective study of 663 KT patients [9].

Frailty prevalence has also been shown to be present in other organ transplants. In a study [2022] of 217 liver transplant patients with low skeletal muscle mass and elevated MELD scores (a measure of severity of liver disease), men had increased infections [$p = 0.021$] and longer LOS [$p = 0.001$], whereas women had longer hospital LOS [$p = 0.032$] when compared to those with higher skeletal muscle mass. However, survival rates were similar among frail versus non-frail patients [18]. In contrast, Wilson and colleagues reported 45% frailty in 102 lung patients, and frail lung recipients had lower post-transplant survival, with an HR of 2.24, 95%CI: 1.22–4.19, $p = 0.0089$ [19]. Recently, a single-centre prospective cohort study of 231 lung transplant recipients reported that frailty after transplantation was associated with the development of chronic allograft dysfunction [20]. Similarly, it has also been reported in a prospective study of 525 KT recipients that frail patients on mycophenolate mofetil (MMF), the standard immunosuppressant used post-renal transplant, were 1.29x more likely to experience MDR (MMF dose reduction) [21]. Recently, Lorenz et al. published a review article examining frailty in chronic kidney disease, and these authors suggested that potential frailty interventions such as early rehabilitation may be useful [22].

Measuring quadriceps muscle layer thickness (QMLT) using ultrasound (US) represents an emerging form of bedside assessment of the muscle mass of the lower thigh, with validation in the critically ill, community-dwelling elderly and healthy populations [23–26]. US has emerged as a prospective tool to assess muscle mass and quality, as it is portable, inexpensive, and utilizes high-frequency ultrasonic waves to visualize living tissue [26–28]. Furthermore, assessing QMLT using US has shown excellent intra- and inter-rater reliability [29,30]. Bioelectrical impedance analysis (BIA), dual-energy X-ray absorptiometry (DEXA), computerized tomography (CT), and magnetic resonance imaging (MRI) are also tools used to assess muscle quantity, with the latter two being able to also assess the quality of the muscle. However, these tools are costly and not available in all clinical settings. Thus, the assessment of QMLT has the potential to serve as a relatively inexpensive screening tool for identifying patients who may be frail. Therefore, the relatively low cost and wide availability of point-of-care ultrasound make this modality an attractive tool to explore and to identify patients at risk for poor outcomes, and it should be utilized with kidney and kidney–pancreas transplant patients.

A clinical decision strategy involving all members of the healthcare team to assess patient suitability for organ transplantation is the standard of care. The purpose of this pre-transplant assessment is to minimize morbidity and mortality post-surgery. Length of stay (LOS) is a metric of patient outcomes that is associated with reduced global healthcare costs and is an objective marker of how quickly patients recover after surgery. In a large

multicenter trial of kidney transplants, patients identified as frail at the time of evaluation had a 1.6-fold increase in LOS, vs. non-frail patients [31].

2. Purpose

Previous research has not been conducted examining QMLT in patients undergoing kidney transplantation. Moreover, research has not fully considered if using US to assess QMLT can identify those at risk for longer hospital lengths of stay in this patient population. Thus, the purpose of this study was to assess whether pre-operative QMLT values are associated with prolonged length of stay in hospital (LOS; defined as >14 days) following renal transplantation. It was hypothesized that pre-transplant patients with lower measures of QMLT would have longer LOS following transplant, as well as higher rates of infection and rejection in the early post-transplant period.

3. Methods

This was a prospective observational cohort study performed at a large academic teaching hospital, in Ontario, Canada. Patient recruitment occurred from 1 March 2019 until 1 January 2020, and all patients presenting for a kidney or combined kidney–pancreas transplant were invited to participate. Patients were excluded if they were under 18 years of age, receiving a concurrent liver or heart transplant, or refused to participate. Upon recruitment, patients provided written informed consent to participate, at which point data collection occurred, which included, age, gender, height, weight, BMI, type of donor (donation after brain death (DBD), donation after circulatory death (DCD), living donor (LD)), panel-reactive antibody (PRA%), Physical Frailty Phenotype scores, and quadriceps muscle layer thickness (QMLT).

The Physical Frailty Phenotype was assessed using the gold-standard criteria set out by Fried et al. (2001) [14]. Components of the frailty phenotype included patients' reported unintentional weight loss of >10% over the last year, self-reported exhaustion, weekly physical activity, hand grip strength assessed with a Jamar dynamometer, and time to walk 15 feet at one's usual pace. Gender and BMI stratified cut-offs used in clinical practice were utilized for assessing the presence or absence of each frailty component. A composite score of >2 indicated the presence of frailty.

QMLT is a measurement of the anterior thigh-compartment musculature comprising the rectus femoris muscle and the vastus intermedius muscle. Point-of-care ultrasound (BK technology, ®Burlington, MA, United States) was used to quantify this value. With the patient in the supine position and feet pointed forward, a tape measure was used to measure the distance from the anterior superior iliac spine to the superior border of the patella, and the halfway point was marked with indelible ink on the anterior aspect of the thigh in the midline of the lower limb. A curvilinear probe set to 6 Hz and with ample ultrasound jelly assessed this point of the thigh musculature. The depth was adjusted so the femur and superficial adipose were visible at the bottom and top of the ultrasound image, respectively. Light pressure was applied to observe tissue dispersion to confirm the discrimination of the visible layers as muscle versus adipose. Pressure was released to the point of minimal pressure from the probe, allowing contact with the probe to the skin, with no external compression applied. The image was then frozen, and electronic calipers measured the vertical distance from the inner layer of the rectus femoris muscle fascia to the level of the femur periosteum to obtain the QMLT. This measurement was repeated for a total of three measurements and then repeated on the contralateral thigh. The mean value of the six measurements obtained comprised the patient's QMLT value.

Patients were then followed prospectively for outcome assessment. The primary outcome of interest was the length of stay in hospital following transplant, which was assessed both as a continuous variable and as a nominal variable of greater than/equal to or less than 14 days. Secondary outcomes of interest included the occurrence of infectious complication, rejection, and renal function at 1 month post-transplant, as measured using serum creatinine level; infection and rejection assessment was limited to the first month

after transplant. Infection was deemed present if the following criteria were met: culture evidence of microbial infection with clinical symptoms and/or treatment with antimicrobials, or radiographic evidence of infection with clinical symptoms and/or treatment with antimicrobials. An infection was not considered present if a patient was treated with a course of antibiotics for prophylaxis or for pre-emptive treatment of a possible donor-derived pathogen. Rejection was documented if there was a biopsy post-transplant documenting graft rejection in the presence of graft dysfunction and treatment provided directed at rejection. Graft function was categorized as delayed if dialysis was required within 7 days of transplant and was otherwise deemed immediate.

Statistical analysis was carried out using SPSS v 29.0. Demographic data were summarized using descriptive statistics. QMLT values were organized by percentile. A cut-off of the 20th percentile was used to divide patients into two categories of QMLT (low and higher). Kolmogorov–Smirnov testing assessed for assumptions of normality, and the continuous outcomes were compared using a two-sided t-test or Mann–Whitney U test where appropriate. Chi-square analysis and Fisher exact testing for nominal variables were performed. Multivariable regression assessed the predictive impact of QMLT on LOS while controlling for relevant variables. Alpha was set at 0.05 and all analyses were two-tailed. An a priori sample size of 74 was chosen to allow for assessment of the difference in LOS using an unpaired t-test using G*Power v 3.1 software, with an effect size of 0.67 based on local data on LOS (mean LOS = 9.0 days, S.D. = 4.5, with a 3-day difference in LOS being deemed clinically significant). For the purposes of multivariable regression to be performed on 5 variables of interest, using the guide of 15 patients per variable of interest, a sample size of at least 75 was sought. We, therefore, aimed to accrue up to 88 patients to allow for a 10–20% rate of attrition. Patients lost to follow-up due to early structural graft loss or death were not included in the assessment of our stated outcomes.

4. Results

During the study accrual period, a total of 85 patients provided consent to participate, with 79 patients providing complete data for analysis. Baseline data are presented in Table 1. The cut-off value to define the two QMLT groups at the 20th percentile was determined to be 2.63 cm. The range of QMLT was 1.09–6.50 cm. A decision was made before data analysis to separate the QMLT into <20% and >20%, as there are no current established cut-off points or adequate muscle mass in kidney recipients. In a previous study by Janssen et al. (2002), NHANES III participants aged 18–39 comprised the referent population, and those in the older age groups (39+) were stratified using Skeletal Muscle Index (SMI), and those between 1 and 2 standard deviations below the referent population were deemed moderately sarcopenic, while those greater than 2 standard deviations below were severely sarcopenic; we therefore utilized this strategy for our study [32].

A comparison of the outcome measures based on QMLT group is outlined in Table 2. Kolmogorov–Smirnov testing determined that LOS, PRA%, and creatinine at 1 month violated assumptions of normality and were therefore compared non-parametrically using Mann–Whitney U test. All other continuous variable satisfied assumptions of normality.

LOS of over 14 days were significantly higher among those with lower QMLT. Additionally, the LOS was significantly longer in the low-QMLT group (12.0 vs. 8.0 days, $p = 0.04$). The difference in distribution for the type of donor (living, DCD, DBD) approached significance ($p = 0.052$) in favor of fewer living donors in the low-QMLT group. The remaining demographic variables did not differ between the groups, nor did the secondary outcomes of rates of infection, rejection, or creatinine at one month. Notably, the breakdown of frailty phenotype scores did not differ between the groups (Table 2). Given that there was an apparent discrepancy in the rates of living donors between the low- and high-QMLT groups (7% vs. 40%), we repeated the comparisons, excluding living-donor recipients. The results for this analysis are displayed in Table 2. When LOS was categorized into >14 d or $\leq$14 d, the difference was preserved (23% vs. 0%, $p = 0.01$). The difference in

mean LOS was no longer significant after the exclusion of living-donor recipients (12.0 vs. 9.0 days, $p = 0.22$). This subsequent analysis carried a power of 36%, as calculated post hoc.

Table 1. Demographic and outcome data for cohort of ESRD patients undergoing kidney transplant.

	Mean	**S.D./%**
N	79	
Age	49.9	14.4
Gender (%M)	51	65%
BMI	28.7	5.5
QMLT (cm)	3.66	1.14
20%ile QMLT	2.63	
LOS (days)	8.7	4.2
Infection (N)	19	24%
Rejection (N)	5	6%
Frailty score (median)	1	
0	22	28%
1	28	35%
2	12	15%
3	8	10%
4	5	6%
Unknown	4	5%
DGF	17	22%
Donor type		
LD	27	34%
DBD	29	37%
DCD	23	29%
SCD	68	86%
ECD	11	14%
Cr 1 month	138	91
%PRA	25%	38%
Transplant (KTx/SPK) (K(KTx/SPK)	73/6	92%/8%

LD = living donor; DBD = donation after brain death; DCD = donation after circulatory death; SCD = standard-criteria donor; ECD = extended-criteria donor; DGF = delayed draft function; KTx = kidney transplant; SPK = simultaneous pancreas/kidney transplant; PRA = panel-reactive antibody; Cr = Creatinine; QMLT = quadriceps muscle layer thickness; ESRD = End stage renal disease.

Multivariable analysis to assess for contributors to LOS was performed with the entry of five variables of interest: QMLT, age, graft function (delayed vs. immediate), frailty phenotype score, and donor type. Because the LOS violated the assumptions of normal distribution, the LOS was log-transformed for multivariable regression. Overall the model constructed was significantly predictive of LOS, with $R^2 = 0.33$, $F(5,74) = 8.89$, $p < 0.001$. The factors of deceased donor and presence of DGF conferred significant regression weight for the prediction of greater LOS (Table 3). Of interest, when we collapsed all the types of deceased donors and compared them to living donors, the QMLT and LOS remined statistically significantly different. Higher QMLT [$p = 0.025$] and shorter LOS [$p = 0.005$] were seen in the living vs. the deceased donors (data not shown). Furthermore, we conducted a deeper dive into the participants with LOS > 14 days and did not find any unique differences in age, gender, BMI, QMLT, or frailty scores (data not shown).

Table 2. Outcome data of ESRD kidney transplant recipients between low- and higher-QMLT cohorts after censoring of living-donor transplant recipients.

	<20%ile QMLT	>20%ile QMLT	*p* Value
N	13	39	
Age (mean)	54.8 (13.7)	49.9 (15.4)	0.5
Gender (%M)	10 (77%)	22 (56%)	0.324
LOS	12.0 (7.4)	9.0 (2.6)	0.22
LOS > 14 d	3 (23%)	0 (0%)	0.01
Infection	2 (15%)	11 (28%)	0.48
Rejection	2 (15%)	2 (5%)	0.26
DGF	31%	33%	0.68
BMI	28.3 (4.9)	29.5 (5.3)	0.31
LD	0 (0%)	0 (0%)	0.63
** DBD	8 (62%)	21 (54%)	
DCD	5 (39%)	18 (46%)	
SCD	10 (77%)	31 (80%)	1.0
ECD	3 (23%)	8 (21%)	
Frailty score			0.77
0	3 (23%)	11 (30%)	
1	5 (39%)	16 (43%)	
2	3 (23%)	7 (19%)	
3	2 (15%)	2 (5%)	
4	0 (0%)	1 (3%)	
Cr 1 month	155 (102)	146 (112)	0.89
PRA	37% (45%)	29% (38%)	0.4
QMLT	2.05 (0.45)	4.00 (0.92)	

All data are presented as N (%) or Mean (S.D.). ** DBD = donation after brain death; DCD = donation after circulatory death; SCD = standard-criteria donor; ECD = extended-criteria donor; DGF = delayed graft function; KTx = kidney transplant; SPK = simultaneous pancreas/kidney transplant; PRA = panel-reactive antibody; Cr = creatinine.

Table 3. Multivariable regression data for length of stay (log-transformed).

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% Confidence Interval for B	
	Beta	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	1.742	0.219			0	1.305	2.178
QMLT	−0.02	0.035	−0.056	0.95	0.566	−0.09	0.05
* Graft function	0.258	0.08	0.327	1.39	0.002	0.097	0.418
Age	0.004	0.003	0.142	1.15	0.153	−0.001	0.009
Living vs. deceased	0.25	0.087	0.305	1.36	0.005	0.077	0.423
Frail vs. not frail	−0.104	0.09	−0.111	0.89	0.253	−0.283	0.076

* Graft function refers to delayed graft function compared to immediate graft function. Living vs deceased donors. Std.Error: Standard Error. T: total using multiple independent variable analysis.

5. Discussion

In this single-centre prospective cohort study of kidney and kidney–pancreas transplant recipients, QMLT was used as a novel assessment tool for identifying patients at risk for prolonged LOS in hospital. Sarcopenia, described as low muscle mass and strength and

measured as QMLT via ultrasound, can lead to frailty, which is associated with negative health outcomes. Recent research suggests that QMLT (consisting of the rectus femoris and vastus intermedius) complexes can be assessed with US, and importantly, QMLT loss may appear prior to whole-body-level loss [26,33,34]. Overall, those with a low QMLT, defined as measuring below the 20%ile of the cohort, demonstrated a significantly greater proportion of LOS over 14 days (21% vs. 3%, $p = 0.04$), as well as a longer mean length of stay in hospital (12.0 vs. 8.0 days, $p = 0.04$) [35].

This difference in LOS may be due to QMLT being representative of frailty. The components of the frailty phenotype include weight loss, slow walking speed, exhaustion, reduced activity, low hand grip strength [14]. The prevalence of frailty was 16% overall (defined as a frailty phenotype score > 2), and this appears to be in keeping with other reports. A large multicentre study of frailty among 3939 kidney transplant candidates enrolled at the time of evaluation and 1291 enrolled at time of admission reported that 18% of patients on the waitlist and 20% who had a kidney transplant were frail [36,37]. Similarly, the US National Database reported that 16.4% of kidney transplant candidates and 14.3% of kidney recipients were identified as frail [16]. Given that these measures are derivatives of skeletal muscle use, it stands to reason that frailty may be coexistent with significant loss of skeletal muscle mass. This could be reflected in the observed quadriceps muscle layer thickness if enough muscle mass was lost overall, and it has been reported in some patient populations. In community-dwelling elderly and critically ill populations, QMLT has been shown to moderately correlate with the lower-limb and total fat-free mass derived from whole-body assessments [25,26].

Frailty in patients with chronic disease and in transplantation represents a significant ongoing issue. Fitzpatrick and colleagues reported that 52% of dialysis patients were frail [15,38], utilizing SRTR data linked to local institutional data to create a hybrid registry-augmented regression model to precisely estimate the impact of several donor and recipient factors with the ability to estimate the influence of frailty. They reported that frail kidney transplant recipients had a six-fold increase in early hospital readmissions, a nine-fold increased risk of delayed graft function, and a three-fold increased risk of immunosuppressive intolerance [21,39,40]. Similarly, a prospective study of 537 kidney transplant recipients who were evaluated at the time of transplant reported that 5-year survival rates for non-frail, intermediary frail, and frail patients, respectively, were 91.5%, 86%, and 77.5% [9]. Furthermore, frailty has been associated with a longer length of stay after transplant. Through this same SRTR analysis, frailty conferred a 1.6-fold higher risk of being hospitalized longer than 2 weeks after transplant [15]. We also observed that lower QMLT was associated with a higher risk of LOS > 14 days. We did not observe an association between frailty phenotype scores and LOS in either pooled analysis or in multivariable regression in our cohort. This may relate to the lower prevalence of frailty in our cohort, which may limit the ability to adequately assess this relationship. With a greater number of patients powered to test the relationship between QMLT and frailty phenotype, a clearer association may emerge. However, emerging evidence indicates that kidney recipients with even mild frailty have increased mortality. A large retrospective study of 296 kidney recipients, after conducting multivariate analysis, reported that patients identified as having only one PFP frailty criterion (mild frailty) had an increased risk of mortality post-transplantation [HR 3.52, 95% CI: 1.03–15.9, $p = 0.048$] [41].

The rates of the secondary outcomes of infection, rejection, and creatinine at 1 month were not significantly different between the low- and high-QMLT groups. It was hypothesized that QMLT may represent a surrogate marker of frailty, thus representing a state of systemic inflammation and inability to withstand extra stressors. Given the known derangements of inflammatory markers such as IL-6 in frail populations, we hypothesized greater rates of infection and rejection [27]. As a result, rates of clinically relevant episodes of infection and rejection were assessed according to QMLT group. QMLT in our cohort was not a robust discriminator of these events. There was a relatively low event rate of rejection overall (6%); thus, a larger sample size may help better define the influence of

QMLT on rejection. Rates of readmission after kidney transplant in larger series, often due to infection or rejection events, have shown differential rates between the frail and non-frail in other reports [39]. The attendant immunosuppression of all transplant recipients may suppress the influence of frailty on the ability to avoid clinical infection in smaller sample sizes. Thus, a larger study may be able to better clarify the prognostic ability of QMLT for these events.

A significant driver of increased LOS in our cohort appears to be the type of donor and the presence of DGF. The influence of the donor type is first evident in the different rates of donor types between the low- and high-QMLT groups (Table 2). When living donors (LDs) were censored, the significance of the difference in mean length of stay was lost (12.0 vs. 9.0 days, $p = 0.22$), but the proportion of recipients remaining in hospital beyond 14 d remained significantly higher in the low-QMLT group. Eliminating LDs significantly reduced the numbers in each group, and this analysis was subsequently underpowered to detect a difference in mean LOS. It has been shown in other reports that frailty significantly increases the risk of LOS beyond 14 days after kidney transplants [3]. The similar influence of QMLT supports this measure as being potentially indicative of frailty.

The significant impact of donor type on LOS was further clarified by a multivariable regression analysis model using age, graft function, type of donor, frailty status, and QMLT as predictors of LOS. Although both donor type and graft function significantly contributed to regression estimates, this model accounts for only 33% of the residual variation, confirming that other factors not included in this model have appreciable influence on LOS. It may be that with greater numbers, QMLT may demonstrate a clearer influence on LOS, and our sample size was not adequate for logistic regression to assess the odds for LOS > 14 days.

Given that DGF involves dialysis within the first week of transplant, a longer stay in hospital seems natural while waiting to define the progression and trajectory of renal function. DGF has been associated with longer LOS after renal transplant in other series as well [15]. Even in the absence of DGF, deceased-donor transplants may display higher rates of "slow graft function" or a less-than-ideal improvement in renal function without requiring dialysis. This logically leads to longer stays in hospital, and this has been demonstrated in a recent systematic review and meta-analysis of 18 studies indicating that frail kidney transplant patients had a higher rate of DGF [RR 1.80, $p = 0.05$] and a longer length of stay [OR 1.64, $p = 0.05$] [42]. Furthermore, research has shown that measuring frailty in pre-kidney-transplant patients was associated with lower graft loss [IRR = 0.71, 95th % CI: 0.54–0.92]; however, no association was seen with mortality [43].

QMLT is a direct measure of one muscle compartment. Although it was predictive of prolonged LOS, it may not be sensitive enough to adequately reflect clinical frailty. Rather, QMLT may more clearly represent a measure of sarcopenia, or pathologic loss of muscle mass. As stated previously, sarcopenia is likely a part of the underlying pathophysiology leading to frailty, resulting in poor health outcomes [13,44].

The discrepant rates of donor types in the low- and high-QMLT groups may also underscore an unappreciated bias in selecting patients for transplant. It is possible that QMLT may be correlated to some other factor not captured within this study that reduces a patient's likelihood of having or being approved for a living-donor transplant. This is another area deserving of further study.

There are some limitations to this study. Overall, this was a single-centre study, which limits the representativeness of this patient population. Also, we may have overlooked other confounders which affected our main clinical outcome. The current study was powered to detect meaningful differences in LOS and allow for multivariable regression; however, the relatively small sample size prevented meaningful subgroup analysis. As well, QMLT provides a metric of muscle size, but it does not measure muscle quality. Fat infiltration of the muscle may be subjectively evident during US assessment of the QMLT by making the muscle appear brighter, but in our current model of QMLT assessment, qualitative assessment of muscle was not incorporated. Future studies investigating the utility of QMLT should consider integrating muscle quality into QMLT assessment. Lastly,

QMLT measures one compartment of the appendicular musculature, and further research is needed to validate this measurement as a marker of sarcopenia in this population. One could argue that analyzing our data as <20% for QMLT is not ideal. However, this decision was made before data analysis was conducted, and currently, there are no established cut-off points for adequate muscle mass, as measured using US, in kidney recipients, thus leaving us with minimal options.

In summary, sarcopenia, measured as low muscle mass and muscle strength, can lead to frailty. Frail kidney transplant patients have negative health outcomes, including increased lengths of stay and increased morbidity and mortality, among others. Identifying frailty in this patient population can be achieved using a validated tool such as the Physical Frailty Phenotype. Most encouragingly, our results may provide convincing evidence that frailty remains an ongoing issue among kidney recipients, and in addition, research has shown that clinical outcomes improve in this patient population when transplant centres assess frailty [43].

6. Conclusions

This small prospective, observational, single-center cohort study represents one of the first to examine quadriceps muscle layer thickness in the renal transplant population, with a preliminary suggestion that low quadriceps muscle layer thickness may relate to increased length of stay in hospital. However, further research is needed to validate these findings.

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Data Availability Statement: The data that support the findings of this study are available on request from the corresponding authors. The data are not publicly available due to privacy or ethical restrictions.

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Abbreviations

Bioelectrical impedance analysis	(BIA)
Computerized tomography	(CT)
Donation after brain death	(DBD)
Donation after circulatory death	(DCD)

Dual-energy X-ray absorptiometry	(DEXA)
Delayed graft function	(DGF)
Kidney transplant	(KT)
Living donor	(LD)
Length of stay	(LOS)
MMF dose reduction	(MDR)
Mycophenolate mofetil	(MMF)
Magnetic resonance imaging	(MRI)
Physical Frailty Phenotype	(PFP)
Panel-reactive antibody	(PRA)
Quadriceps muscle layer thickness	(QMLT)

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