Ultrasound to evaluate muscle quality and quantity in CKD

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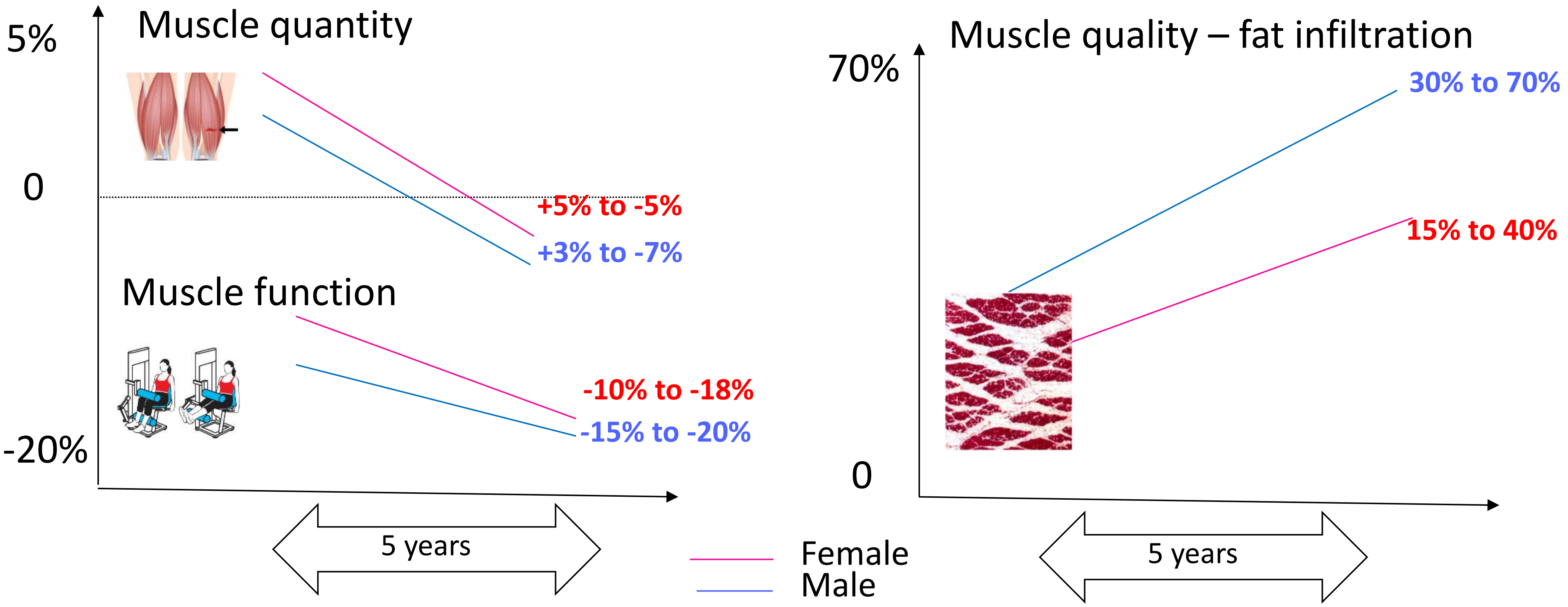
Outline

- Muscle abnormalities
- Evaluating muscle quantity and quality
- Ultrasound for the evaluation of muscle quantity
  - → Reliability/Validity
  - → Utility
- Ultrasound for the evaluation of muscle quality
  - → Validity
  - → Utility
- Practical considerations

Muscle abnormalities related to outcome

Naturally occurring with aging, but also secondary to chronic diseases



Delmonico et al, Am J Clin Nutr 2009;90:1579–85

Muscle fat infiltration

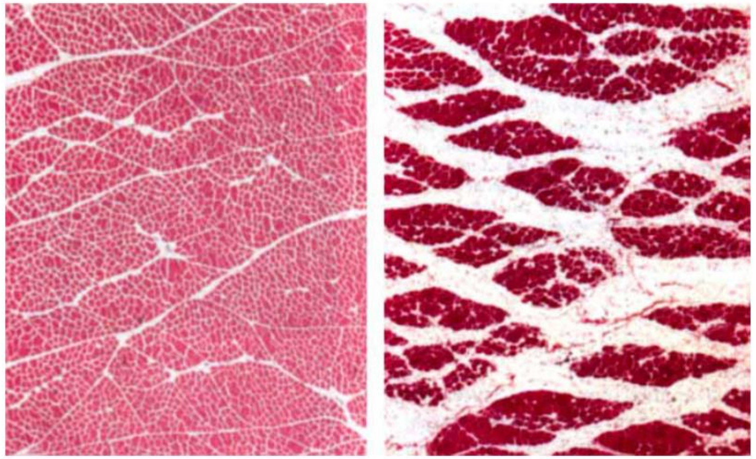
→ Mechanical changes in fiber orientation

→ ↓ elasticity

→ ↓ muscle tension

→ ↓ generate force / muscle contraction

intact | fatty infiltrated muscle



Infiltrating fat and fibrous tissue (white) were found to be interfibrous, filling the gap area created between the muscle fibres.

Meyer et al. J Orthopaedic Research 22, 2004

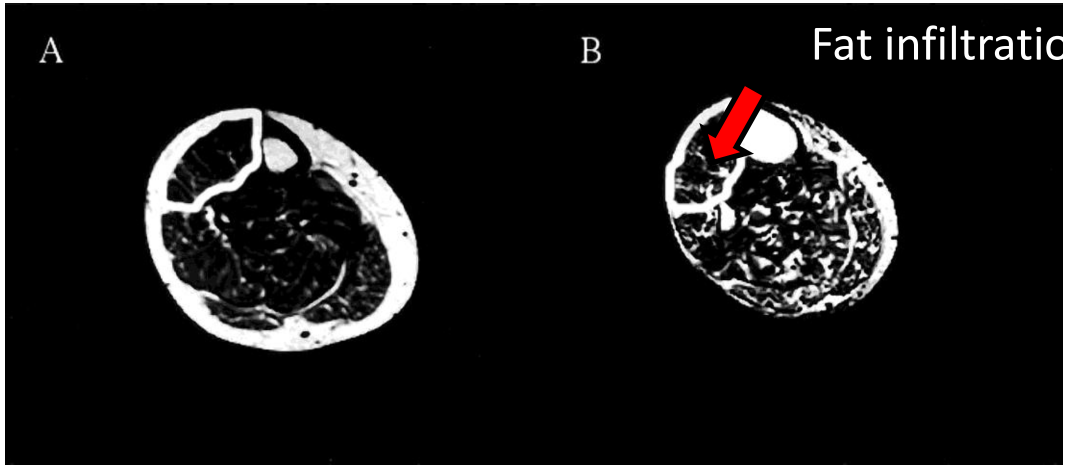
↓ Muscle quality

↓

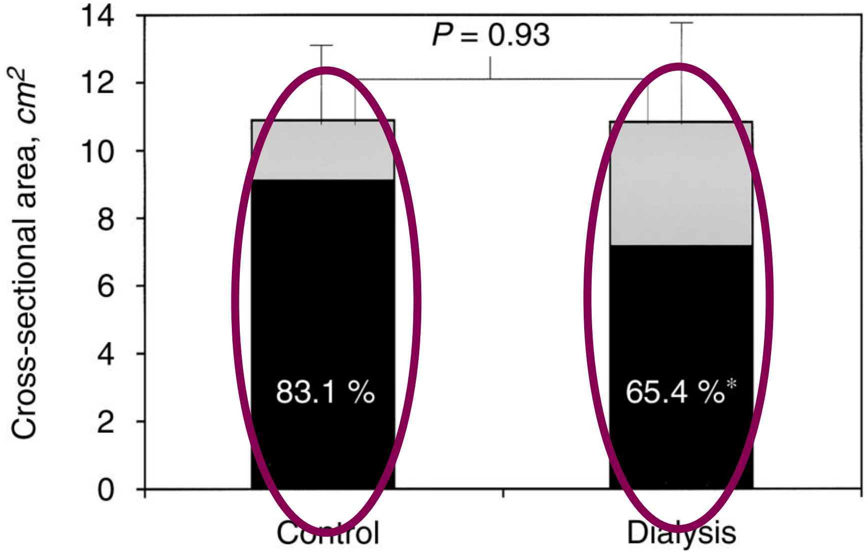
directly affect muscle function

Addison et al, Int J Endoc Article ID 309570, 2014

Lower contractile area in patients on HD in comparison to healthy controls



(A) 72-year-old female control subject.
(B) 70-year-old female hemodialysis subject.



↓ Contractile muscle area
↑ Non-contractile muscle area

Johansen et al, Kidney Int; 63:291–297, 2003

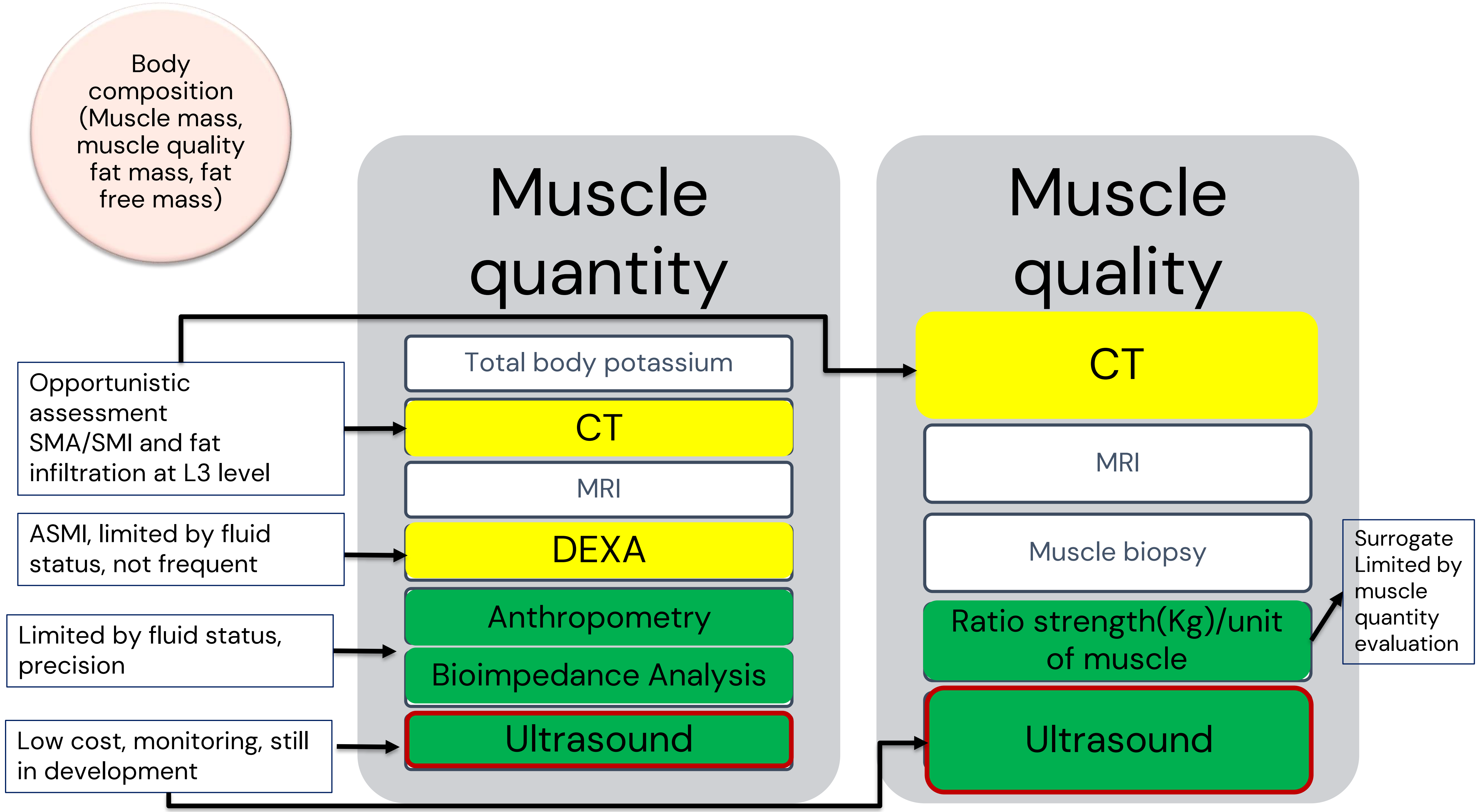
GUIDELINES

Sarcopenia: revised European consensus on definition and diagnosis

Age and Ageing 2018; **0:** 1–16
doi: 10.1093/ageing/afy169

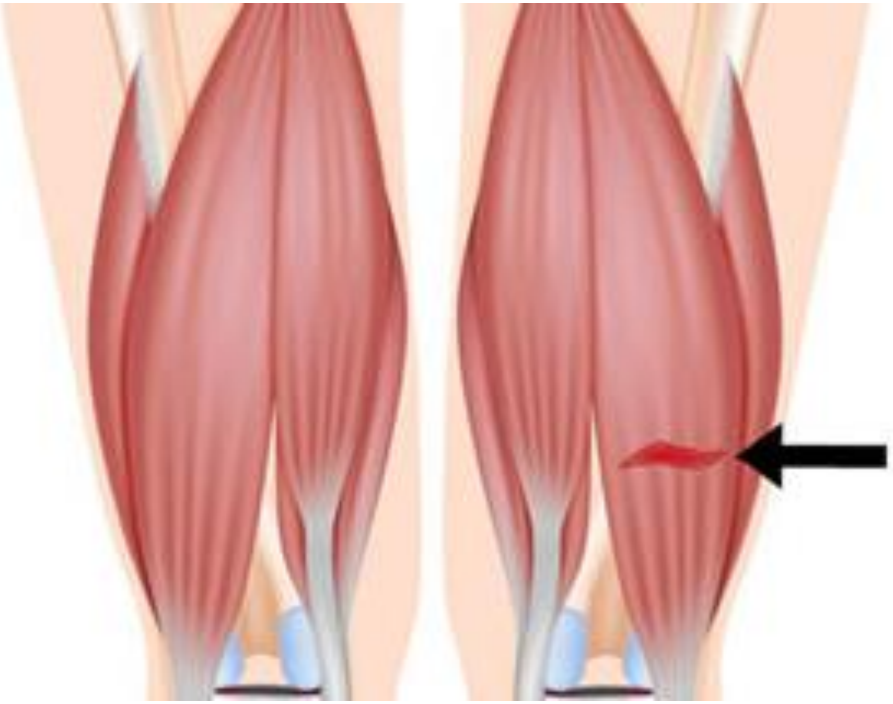
Table 1. 2018 operational definition of sarcopenia

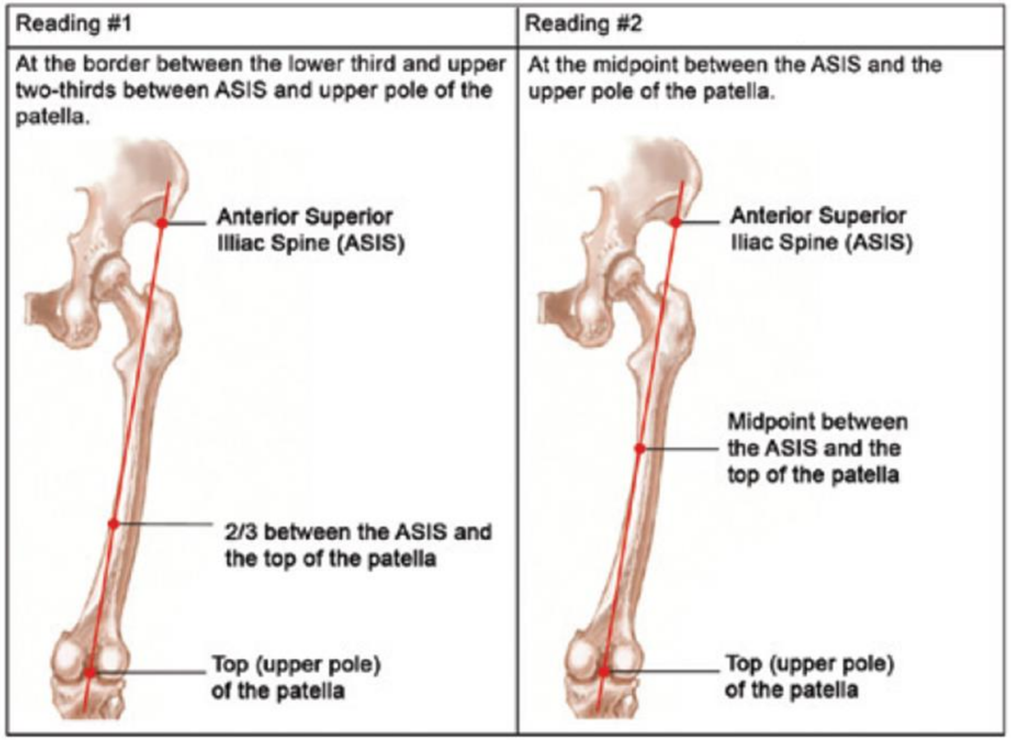
Probable sarcopenia is identified by Criterion 1.
Diagnosis is confirmed by additional documentation of Criterion 2.
If Criteria 1, 2 and 3 are all met, sarcopenia is considered severe.
(1) Low muscle strength
(2) Low muscle quantity or quality
(3) Low physical performance



Body composition (Muscle mass, muscle quality fat mass, fat free mass)
Muscle quantity
Total body potassium
CT
MRI
DEXA
Anthropometry
Bioimpedance Analysis
Ultrasound
Muscle quality
CT
MRI
Muscle biopsy
Ratio strength(Kg)/unit of muscle
Ultrasound
Opportunistic assessment SMA/SMI and fat infiltration at L3 level
ASMI, limited by fluid status, not frequent
Limited by fluid status, precision
Low cost, monitoring, still in development
Surrogate Limited by muscle quantity evaluation

Muscle US:
Which muscle and which point?

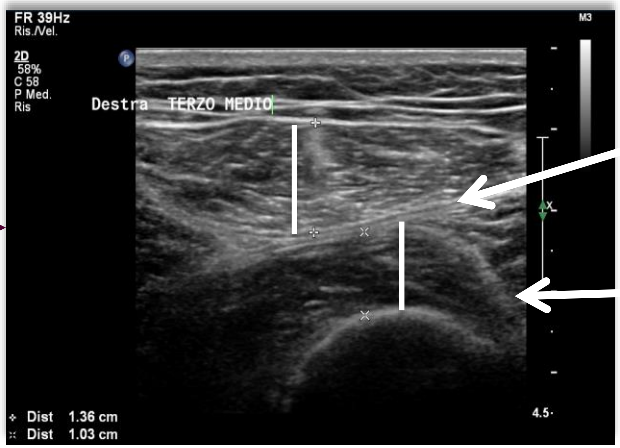




- Lower extremities are affected earlier by age-related loss compared to the muscles of the upper extremities
- Reduction of the anterior thigh muscles occurs at a higher rate compared to the other leg muscles

Janssen I et al. J Appl Physiol (1985) 2000; 89: 81–88
Minetto MA et al. PM R 2016; 8: 453–462

Ultrasound as a valid tool to assess body composition in patients with kidney disease

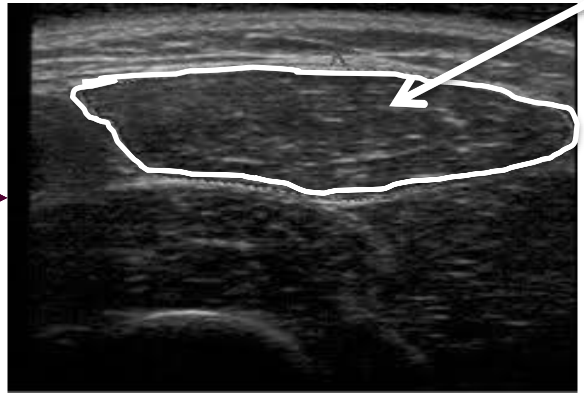


RFT

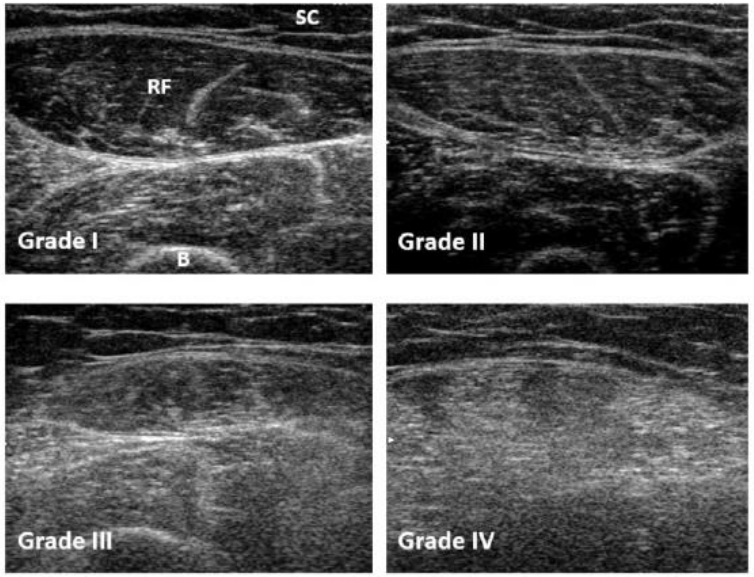
VIT

Muscle quantity

RFCSA



Muscle quality



↑ echogenicity = ↑ fat infiltration

Sabatino A et al Clin Nutr 2017; 36: 1710-1715
Wilkinson et al. Nephrol Dial Transplant (2019) 34: 1344–135

US to assess muscle quantity

The reliability and validity of ultrasound to quantify muscles in older adults: a systematic review

Reliability studies (n = 13), validity studies (n = 6)

Intra-rater reliability: The highest intraclass correlation coefficient (ICC) scores were: vastus lateralis (ICC = 0.852 to 0.999), the rectus femoris (ICC = 0.72 to 0.997), the upper arm anterior (ICC = 0.81 to 0.99), and the trunk (0.73 to 1.00).

Inter-rater reliability (4 studies): Reliability estimates ranged from 0.88 to 0.998

Table 3 Overview of the included validity studies

Study	Demographics[a]	Reference method	Scanning plane	Muscle	Muscle dimension	Validity estimates[b]
Berger *et al.*, 2015[36]	Community-dwelling older adults n = 51 (25:26) age (females) = 72.5 (5.8) age (males) = 74.5 (6.5)	DXA	Transverse	Rectus femoris	Thickness	Right: r = 0.9687 Left: r = 0.9667
Hammond *et al.*, 2014[23]	Ambulatory COPD patients n = 15 (NR:NR) age = NR (NR)	Ultrasound linear transducer	Transverse	Rectus femoris	CSA	ICC = 0.982 (NR)
MacGillivray *et al.*, 2008[24]	Community-dwelling older adults n = 11 (NR:NR) median age = 79	MRI	Sagittal	Rectus femoris	Volume	ICC = 0.997 (NR)
Reeves *et al.*, 2004[29]	Healthy adults n = 6 (3:3) age = 76.8 (3.2)	MRI	Transverse	Vastus lateralis	CSA	ICCs between 0.998 and 0.999 for scans 6 to 10
Sipila and Suominen, 1993[37]	Older adults n = 36 (0:36) Trained athletes n = 21 (0:21) age = 73.7 (5.6) Healthy controls n = 15 (0:15) age = 73.6 (2.9)	CT	Transverse	Quadriceps	Thickness, CSA	Thickness r = 0.761 CSA r = 0.911
Thomaes *et al.*, 2012[33]	Older coronary artery disease patients without cardiovascular incident in the last year n = 20 (NR) age = 68.3 (7.3)	CT	Transverse	Rectus femoris	Thickness	ICC = 0.92 (0.81–0.97)

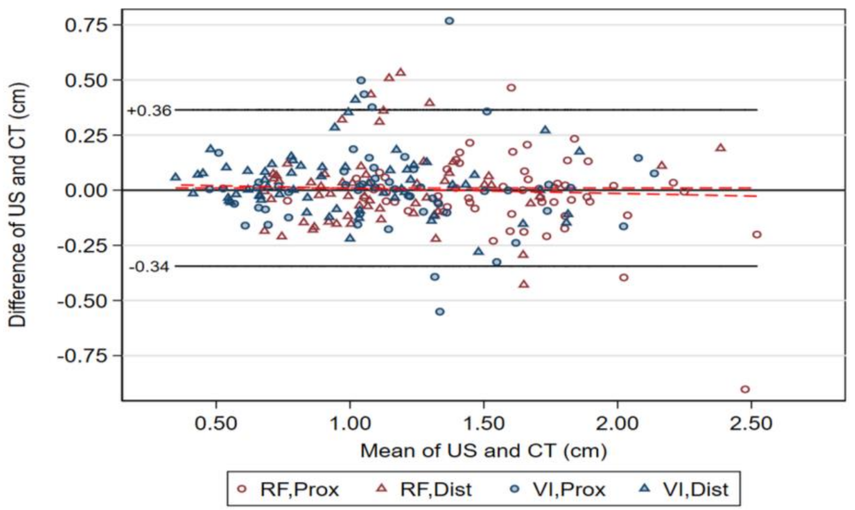
All studies found that ultrasound is valid for the assessment of muscles, with ICC scores ranging from 0.92 to 0.999, and r = 0.761 to r = 0.911.

Journal of Cachexia, Sarcopenia and Muscle 2017; 8: 702–712

Reliability of bedside ultrasound for measurement of quadriceps muscle thickness in critically ill patients with acute kidney injury

Alice Sabatino [a], Giuseppe Regolisti [a], Laura Bozzoli [c], Filippo Fani [a], Riccardo Antoniotti [a], Umberto Maggiore [b], Enrico Fiaccadori [a, *]

Intraobserver reliability: ICC 0.97 – 1.00
Interobserver reliability: ICC 0.88 – 0.93
Test-retest reliability (before and after RRT): ICC = 0.97



Journal of Nephrology
https://doi.org/10.1007/s40620-019-00659-2

ORIGINAL ARTICLE

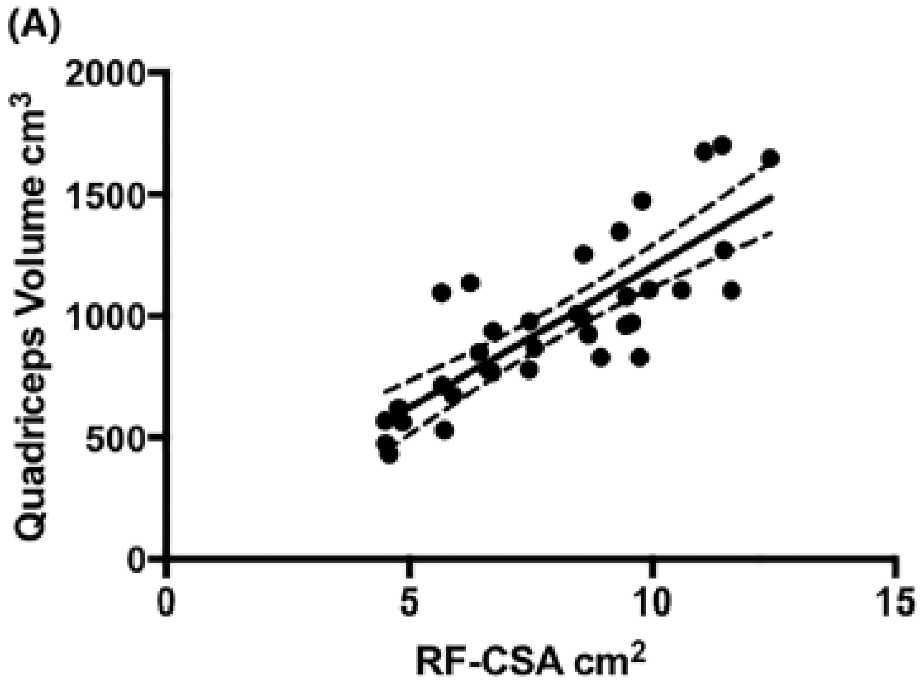
Validation by CT scan of quadriceps muscle thickness measurement by ultrasound in acute kidney injury

Alice Sabatino[1] · Giuseppe Regolisti[1,2] · Francesca di Mario[1,2] · Andrea Ciuni[3] · Anselmo Palumbo[3] · Francesco Peyronel[1,2] · Umberto Maggiore[1,2] · Enrico Fiaccadori[1,2]

- A little less precise than CT, but consistent over time
- The main limitation of US is its lack of standardized protocols and examiner-dependent factors, which can lead to evaluation errors and thus interfere with the reproducibility of results

Clinical Nutrition 36 (2017) 1710–1715

Cross-sectional area quantified by US is highly associated with muscle volume by MRI



Baseline association between RF-CSA (US) and RF volume (MRI):
$r^2 = 0.815$, CI 0.661 to 0.903; $P < 0.001$

Journal of Cachexia, Sarcopenia and Muscle 2019; **10**: 748–755

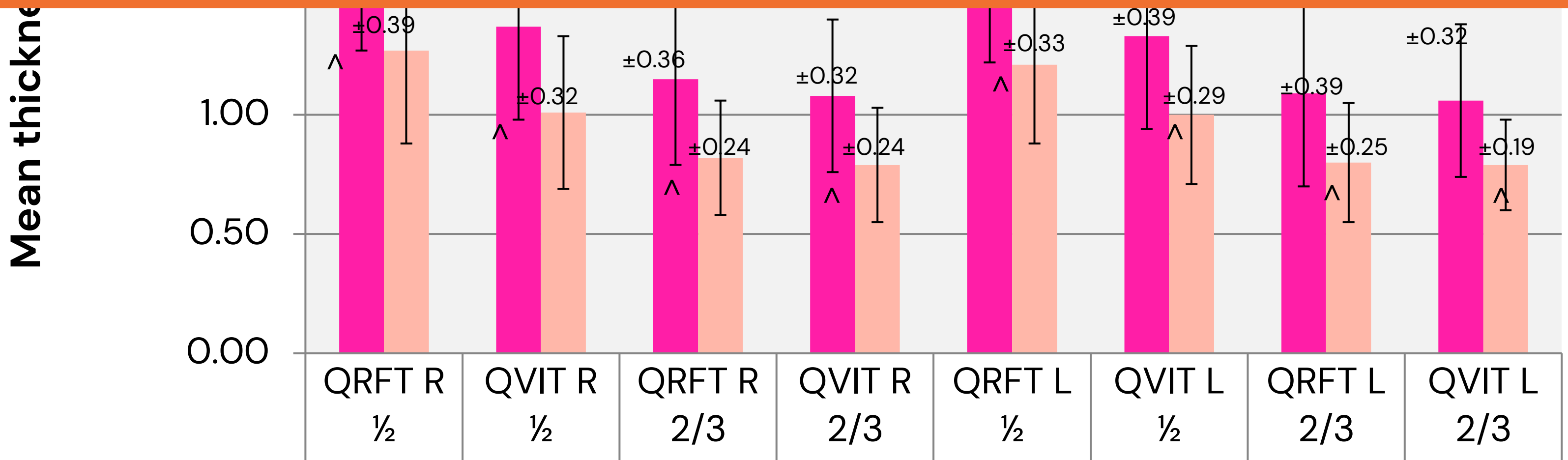
Original article

Noninvasive evaluation of muscle mass by ultrasonography of quadriceps femoris muscle in End-Stage Renal Disease patients on hemodialysis

Alice Sabatino [a], Giuseppe Regolisti [a], Marco Delsante [a], Tommaso Di Motta [b], Chiara Cantarelli [b], Sarah Pioli [c], Giulia Grassi [d], Valentina Batini [e], Mariacristina Gregorini [f], Enrico Fiaccadori [a, b, *]

Can US detect low muscle?

Lower in HD patients with malnutrition



	QRFT R ½	QVIT R ½	QRFT R 2/3	QVIT R 2/3	QRFT L ½	QVIT L ½	QRFT L 2/3	QVIT L 2/3
MIS < 6 (n=68)	1.68	1.37	1.15	1.08	1.64	1.33	1.09	1.06
MIS ≥ 6 (n=53)	1.27	1.01	0.82	0.79	1.21	1.00	0.80	0.79

*Adjusted by age and sex

Clin Nutr. 2019; 38:1232-1239

US was also used to identify patients on HD with PEW

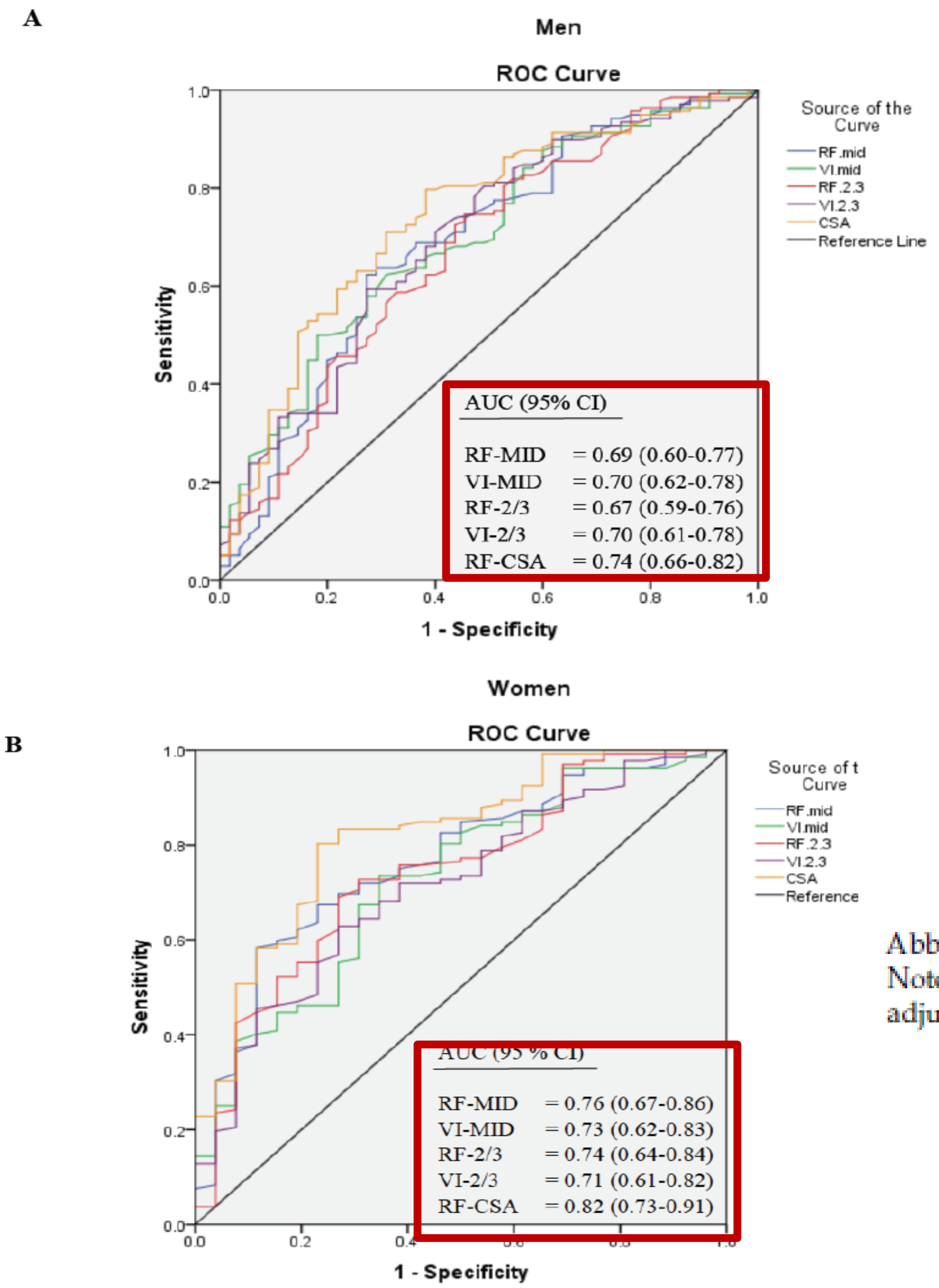


Table 6. Association of the RF_{CSA} gender-specific values with PEW risk.

PEW Risk	Odds Ratio	95% CI	*p*-Value
Unadjusted			
Low RF_{CSA}	8.00	4.62–13.86	<0.001
High RF_{CSA}	Reference		
Adjusted [a]			
Low RF_{CSA}	8.63	4.80–15.50	<0.001
High RF_{CSA}	Reference		

Abbreviations: CI, confidence interval; CSA, cross-sectional area; PEW; protein energy wasting; RF, *rectus femoris*. Note: RF_{CSA} gender-specific values for the PEW risk was < 6.00 cm^2 for men and < 4.47 cm^2 for women. [a] Data was adjusted for age, ethnicity, dialysis vintage, and comorbidities.

Sahathevan S et al Nutrients 2020; 12: 3597

Cut-off values?

Review Article

Ultrasound cut-off values for muscle thickness, cross-sectional area, and echo intensity in Caucasian adults: a narrative review

Jona Van den Broeck[1]^, Savanah Héréus[1]^, Erik Cattrysse[1]^, Hubert Raeymaekers[2]^, Aldo Scafoglieri[1]^

	Author	Participant position	Measurement site	Scan plan palcement transducer	Definition variable	Cut-off	
Rectus femoris muscle							
Muscle thickness	Barotsis *et al.* [2020] (23) Healthy Greece		Midpoint between the ASIS and the superior border of the patella	Transverse	Between superficial and deep aponeurosis of the muscle	1.54	
				Longitudinal		1.59	
	Minetto *et al.* [2016] (27) Healthy Italy					Men	Women
						1.99	1.59
	Rustani *et al.* [2019] (30) Hospital Italy	Supine with extended knees	Halfway between the greater trochanter femoris and the lateral condyle of the femur	Perpendicular to the thigh	Not described	Men	Women
						0.9	0.7
CSA	Fernández-Jiménez *et al.* [2024] (25) Cancer	Supine	One third point between superior border of the patella … ASIS. Midpoint …een the ASIS and …uperior border of	Transverse	Not described	2.7	
	Esme *et al.* [2022] (24) Sarcoidosis Turkey			Perpendicular to the skin		0.0565	

Echo intensity	Arts *et al.* [2010] (22) Healthy western	Supine		Transverse	Region on interest from an area as large as possible without surrounding fascia or bone		Men	Women
						20 y	31	36
						30 y	32	40
						40 y	35	41
						50 y	37	42
						60 y	40	45
						70 y	45	46
						80 y	50	47
						90 y	55	50
	Maurits *et al.* [2003] (26) Healthy The Netherlands	Prone, arms and legs extended	Halfway between the greater trochanter femoris and the lateral condyle of the femur	Transverse and longitudinal; perpendicular to the bone	Not described	Based on age		
						20–30 y	64.23	
						30–50 y	89.02	
						50–70 y	112.55	
						70+ y	139.83	
Vastus intermedius muscle								
Muscle thickness	Barotsis *et al.* [2020] (23) Healthy Greece	Supine	Midpoint between the ASIS and the superior border of the patella	Transverse	Between the aponeurosis and bone-muscle interface	1.01		
				Longitudinal		1.00		

Need for cut-off values that are sex and age-specific.

Cut-offs to evaluate outcome (derived from the population under study) *vs* the effect of age (healthy young) or the disease (healthy old)

Quant Imaging Med Surg 2025;15(4):3665-3

Other cut-offs specific to nephrology

Quadriceps muscle thickness assessed by ultrasound is independently associated with mortality in hemodialysis patients

Alice Sabatino[1,2], Jeroen P. Kooman[3], Tommaso Di Motta[1,2], Chiara Cantarelli[1,2], Mariacristina Gregorini[4], Stefano Bianchi[5], Giuseppe Regolisti[6] and Enrico Fiaccadori[1,2]

→ 181 pts from Italy
Used the median of the distribution

Article

Association of Ultrasound-Derived Metrics of the Quadriceps Muscle with Protein Energy Wasting in Hemodialysis Patients: A Multicenter Cross-Sectional Study

→ 351 pts from Malaysia
Derived from ROC curves with presence of PEW as the reference

Utility of Ultrasound as a Valid and Accurate Diagnostic Tool for Sarcopenia

Sex-Specific Cutoff Values in Chronic Kidney Disease

Thomas J. Wilkinson, PhD, Eleanor F. Gore, MSc, Noemi Vadaszy, MSc, Daniel G. D. Nixon, MSc, Emma L. Watson, PhD, Alice C. Smith, PhD

→ 113 pts from UK.
Derived from ROC curves using low muscle as assessed by ASM, ASMI and ASM/BMI as reference methods (cut-offs from EWGOSP and FNIHS)

Eur J Clin Nutr. 2022;76:1719-1726; Nutrients 2020, 12, 3597; doi:10.3390/nu12113597; J Ultrasound Med 2021; 40:457–467

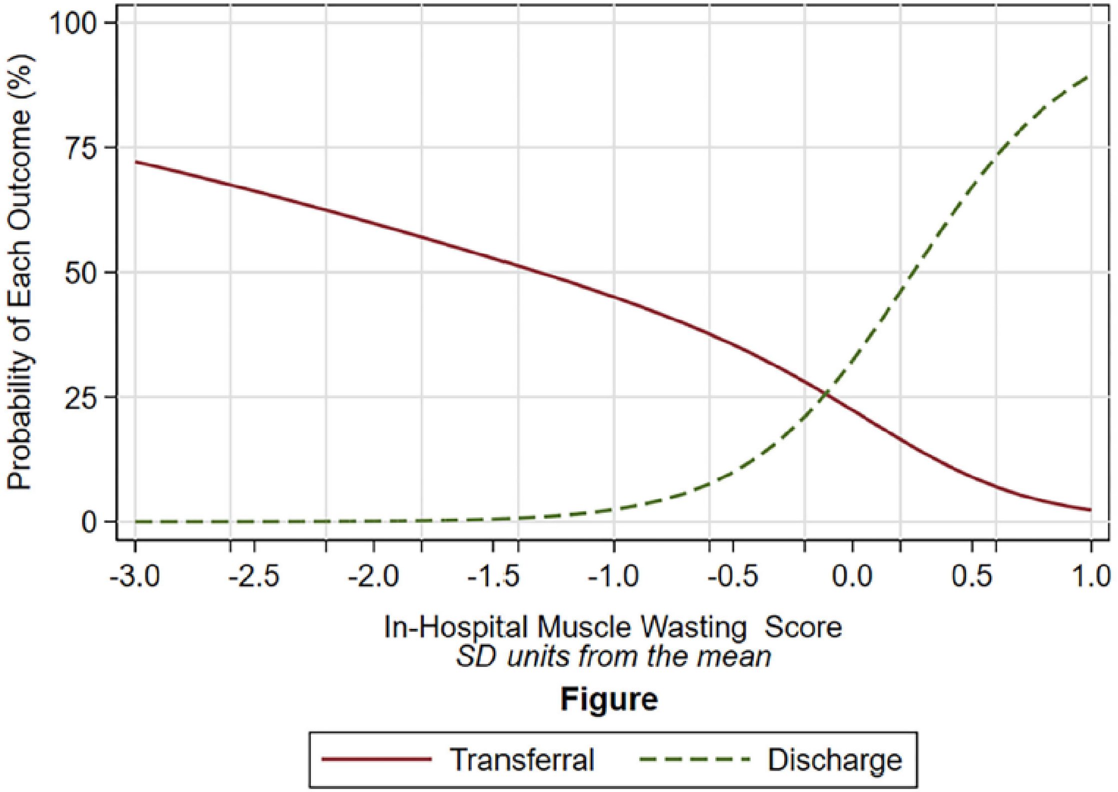
US as a monitoring tool

Ultrasound for Non-invasive Assessment and Monitoring of Quadriceps Muscle Thickness in Critically Ill Patients With Acute Kidney Injury

Alice Sabatino[1,2], Umberto Maggiore[1,2], Giuseppe Regolisti[1,2], Giovanni Maria Rossi[1,2], Francesca Di Mario[1,2], Micaela Gentile[1,2], Maria Teresa Farina[1,2] and Enrico Fiaccadori[1,2]*

[1] UO Nefrologia, Azienda Ospedaliera- Universitaria Parma, Parma, Italy, [2] Dipartimento di Medicina e Chirurgia, Università di Parma, Parma, Italy

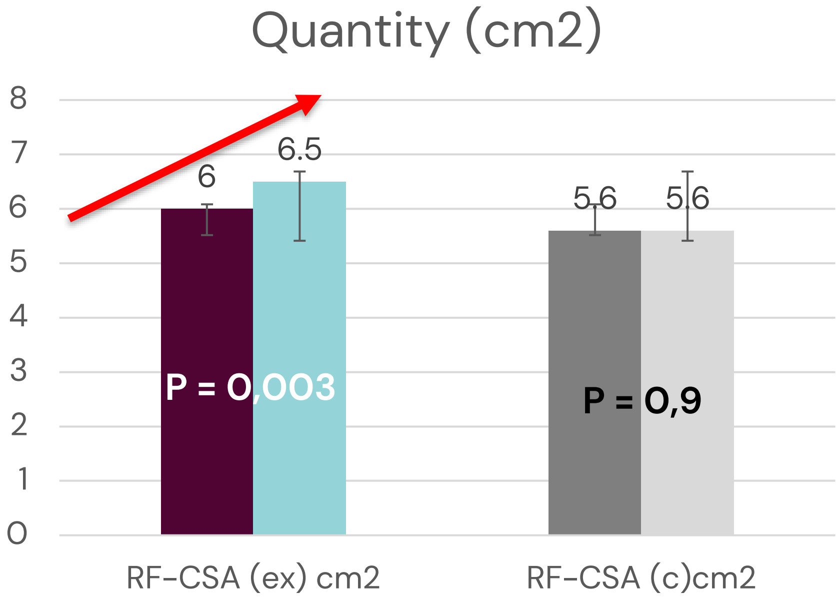
As a monitoring tool:
- Sensible to short-term changes
- Changes associated to outcome

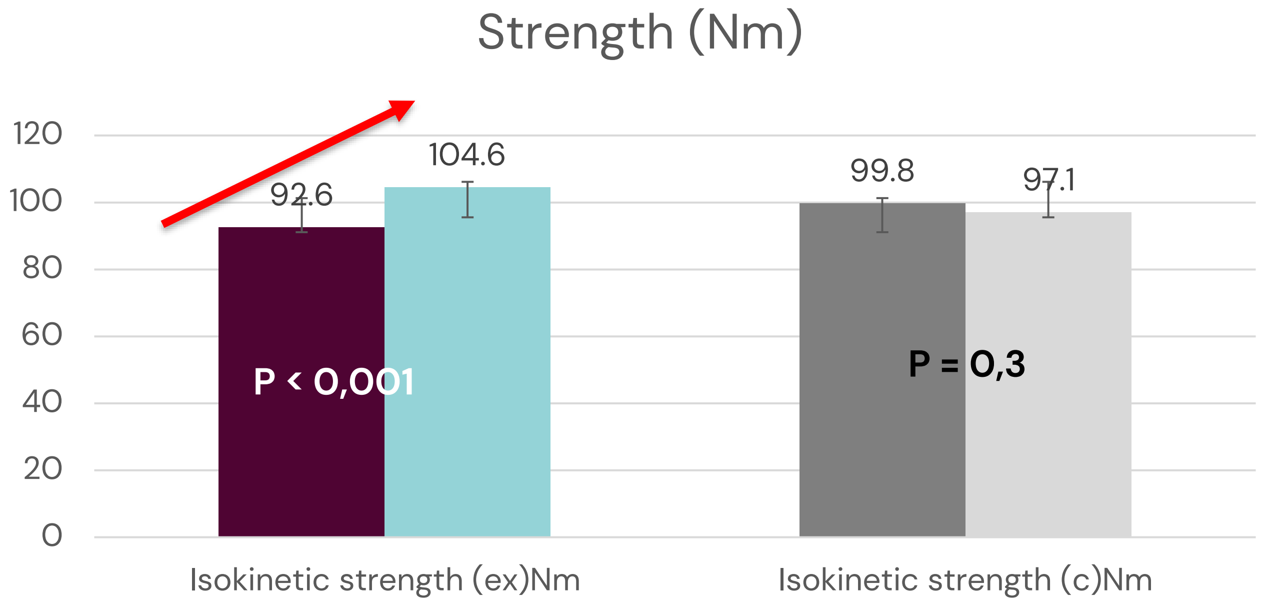


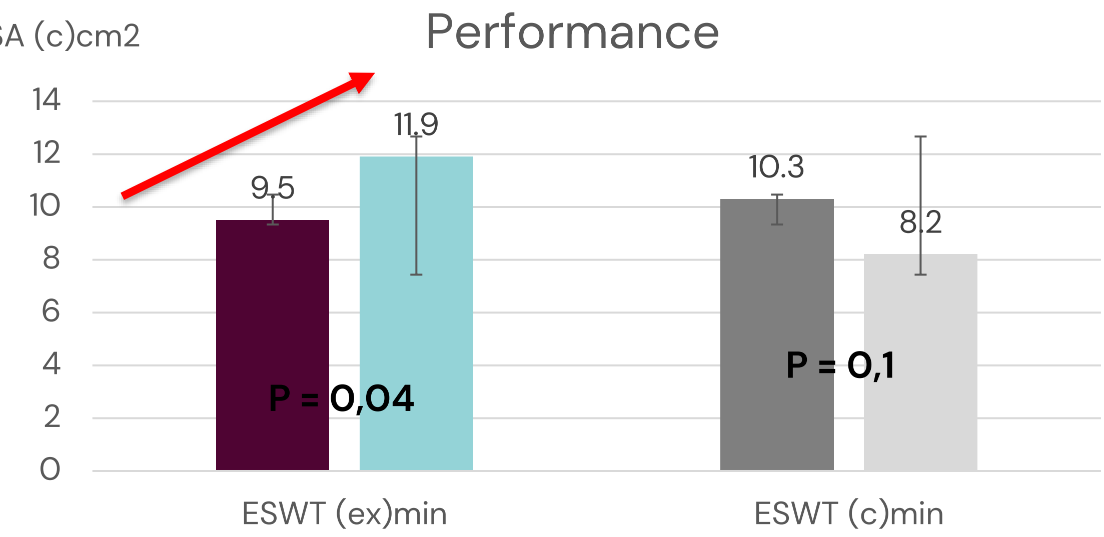
Front. Nutr. 8:622823. doi: 10.3389/fnut.2021.622823

Progressive Resistance Exercise Training in CKD: A Feasibility Study

Emma L. Watson, PhD,[1] Neil J. Greening, MD,[2] João L. Viana, PhD,[3] Jaspreet Aulakh, BSc,[1] Danielle H. Bodicoat, PhD,[4] Jonathan Barratt, PhD,[1] John Feehally, DM,[5] and Alice C. Smith, PhD[1,5]



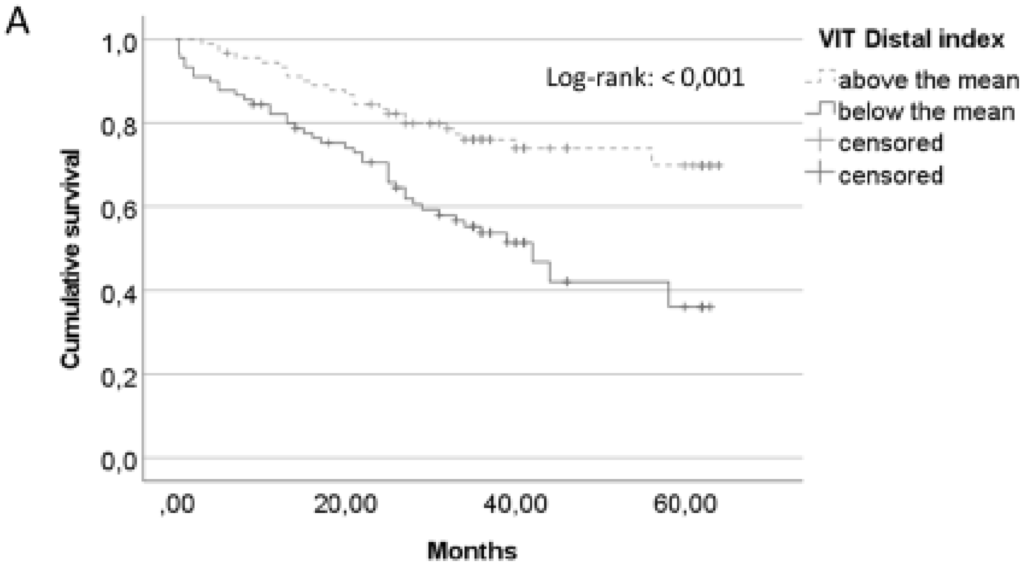


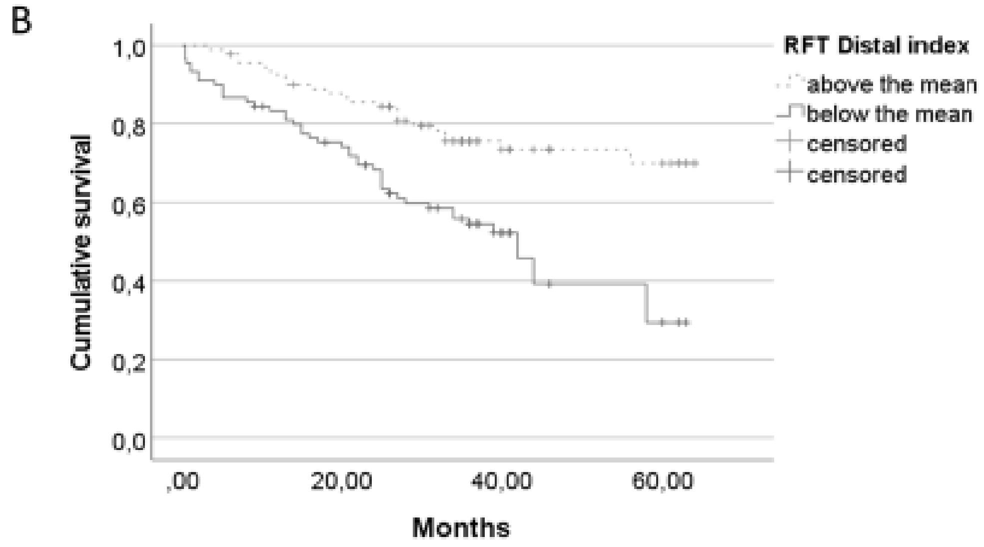


ESWT: endurance shuttle walking test

Am J Kidney Dis. 2015;66(2):249-257

US as a prognostic tool





181 patients, ref value < median of the distribution

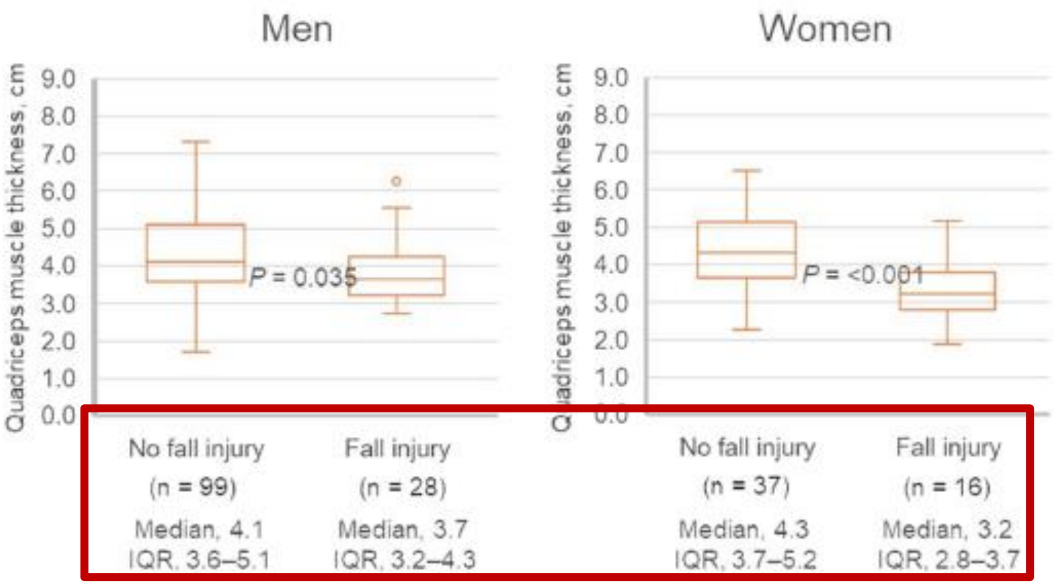
Variables	HR (95% confidence interval); *P*
Univariate analysis	
VIT Distal index below the median	2.41 (1.45–4.00); 0.001
RFT Distal index below the median	2.46 (1.47–4.11); <0.001
Multivariable analysis[a]	
VIT Distal index below the median	1.71 (1.01–2.89); 0.045
RFT Distal index below the median	1.57 (0.90–2.74); 0.113

Adjusted for age, serum creatinine, serum albumin, diabetes and cardiovascular disease.

Eur J Clin Nutr. 2022;76:1719-1726

Quantitative sonographic assessment of quadriceps muscle thickness for fall injury prediction in patients undergoing maintenance hemodialysis: an observational cohort study

Asuka Sai[1], Kentaro Tanaka[2,3,4], Yasushi Ohashi[3*], Akifumi Kushiyama[5,4], Yoshihide Tanaka[6], Shuta Motonishi[7], Ken Sakai[8], Shigeko Hara[9] and Takashi Ozawa[1]



Increased risk of falls in patients with lower total quadriceps muscle thickness

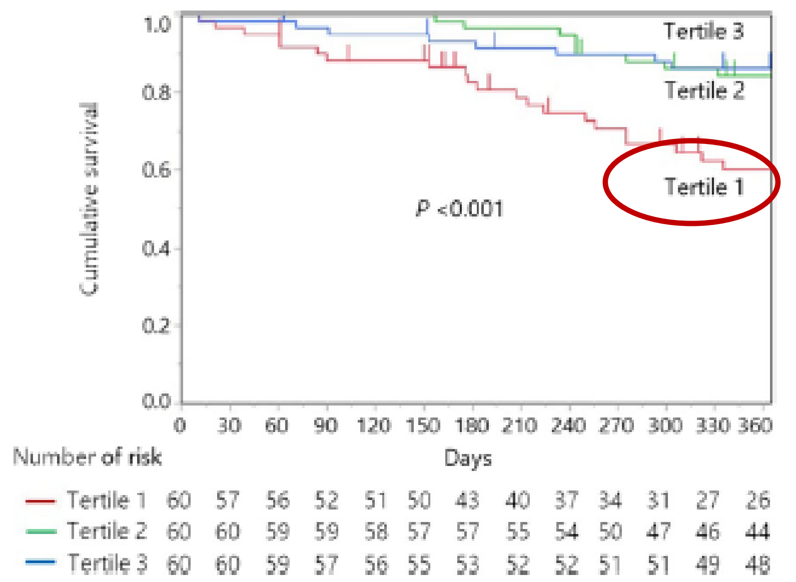
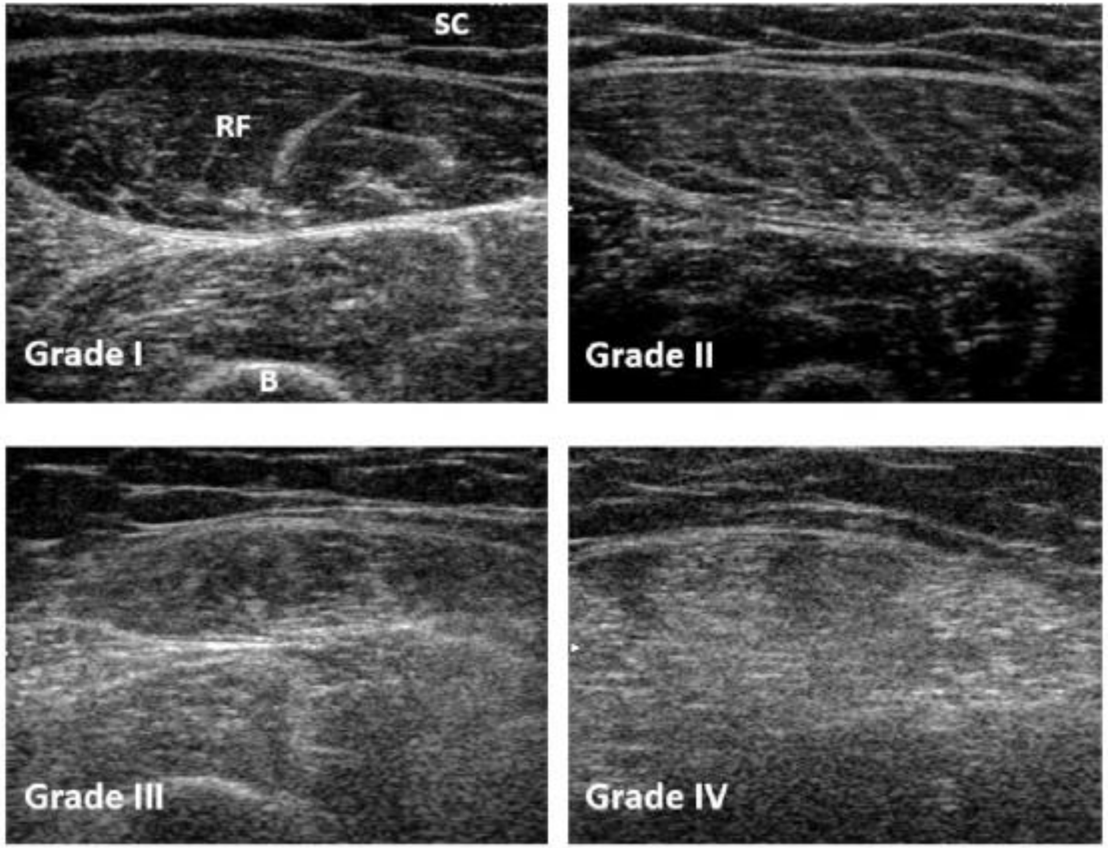


Fig. 3 Kaplan–Meier curves for fall injury by tertiles of quadriceps muscle thickness

Hazard ratio [95% CI], 2.33 [1.22–4.52], P < 0.001

US to assess muscle quality

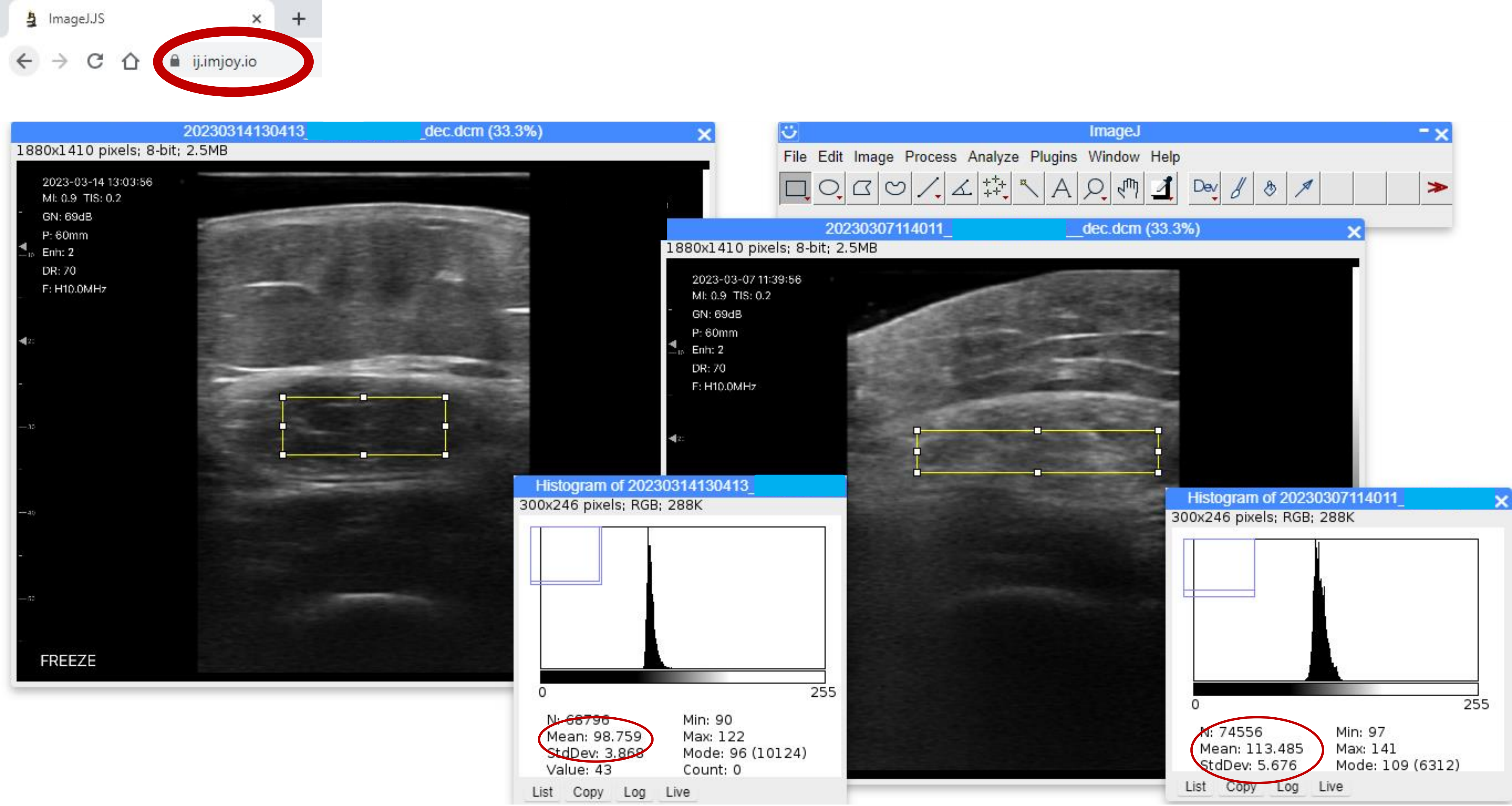


↑ echogenicity = ↑ fat infiltration

Qualitative US assessment of RF skeletal muscle pathology using Heckmatt's scale.

Grade I: US appearance shows predominantly dark RF muscle bordered by subcutaneous fat (SC) and a bright, distinct bone reflection;
Grade II: increased signal in the RF with preserved bone reflection;
Grade III: moderately increased signal and reduced bone reflection;
Grade IV: markedly increased signal and absent bone reflection.

Wilkinson et al. Nephrol Dial Transplant (2019) 34: 1344–1353



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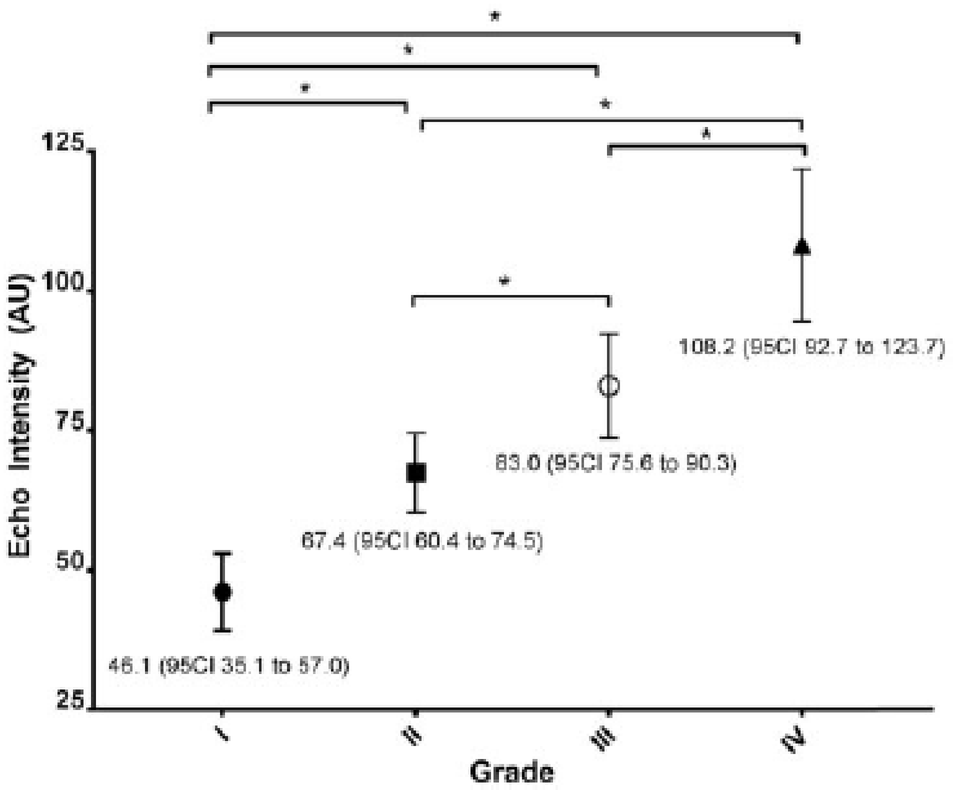


FIGURE 3: EI for each Heckmatt's scale group (Groups I, II, III and IV). Data presented as mean and 95% CI. Significance set at P < 0.050.

- Intra-rater reliability of Heckmatt's: Rater 1, ICC r = 0.769; Rater 2, ICC r = 0.773, both P<0.001)
- Inter-rater reliability: ICC r = 0.760, P<0.001)
- Raters agreed on 84% of the gradings

Wilkinson et al. Nephrol Dial Transplant (2019) 34: 1344–1353

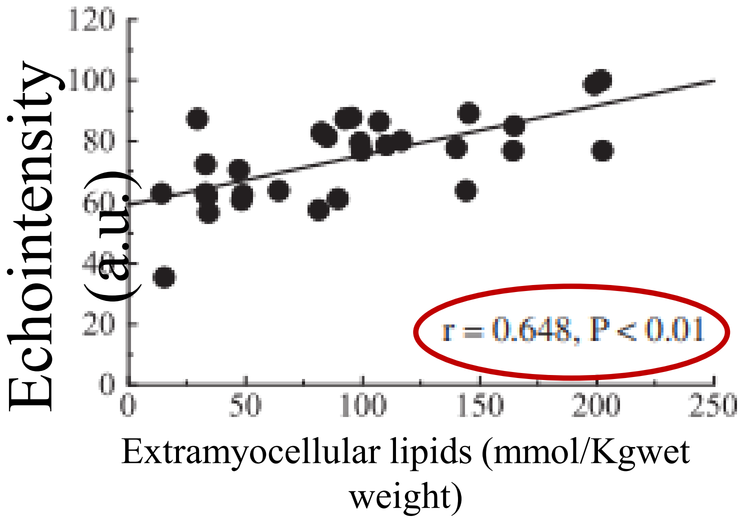
Validation

Original contribution

Intramuscular adipose tissue determined by T1-weighted MRI at 3 T primarily reflects extramyocellular lipids

Hiroshi Akima [a,b,*], Maya Hioki [c], Akito Yoshiko [c], Teruhiko Koike [a,c], Hisataka Sakakibara [c,1], Hideyuki Takahashi [d], Yoshiharu Oshida [a,c]

Magnetic Resonance Imaging 34 (2016) 397–403



Journal of Clinical Medicine

MDPI

Article

The Comparative Associations of Ultrasound and Computed Tomography Estimates of Muscle Quality with Physical Performance and Metabolic Parameters in Older Men

J. Clin. Med. **2018**, 7, 340; doi:10.3390/jcm7100340

Correlation between echo intensity and Intermuscular adipose tissue by CT: r = 0,73 p < 0,001

Monitoring

Table 4
Anthropometric and laboratory data, muscle strength, physical performance, and skeletal muscle mass assessment by ultrasound in older men.

Parameter	T0 (baseline)	T1 (6 months)	T2 (12 months)	p-value
Weight (kg)	69.3 ± 13.8	68.7 ± 13.4	68.0 ± 13.0	0.37
BMI (kg/m^2)	25.6 ± 5.5	24.7 ± 4.1	24.7 ± 4.2	0.16
Serum albumin, g/dL	3.9 ± 0.3	3.9 ± 0.2	3.9 ± 0.2	0.64
nPCR, g/kg	1.07 ± 0.04	1.09 ± 0.05	1.09 ± 0.07	0.32
CC (cm)	31.6 ± 2.1	31.1 ± 1.9	29.6 ± 2.7[b]	< **0.01**[a]
Low CC (n, %)	13 (92.9)	14 (100.0)	14 (100.0)	0.37
HGS (kgf)	24.4 ± 6.5	25.6 ± 7.4	24.8 ± 6.8	0.48
Low HGS (n, %)	11 (78.6)	11 (78.6)	10 (71.4)	0.37
Gait speed (m/s)	0.94 ± 0.10	0.90 ± 0.08	0.84 ± 0.07[b]	< **0.01**[a]
Low physical performance (n, %)	1 (7.1)	1 (7.1)	3 (21.4)	0.14
Muscle ultrasound				
QT (mm)	20.5 ± 1.7	18.8 ± 1.7	16.5 ± 1.4[b]	< **0.01**[a]
RF-CSA (mm^2)	256.0 ± 32.9	229.2 ± 30.0	204.2 ± 25.1[b]	< **0.01**[a]
Echogenicity (0–255)	104.5 ± 4.8	120.2 ± 4.6	143.9 ± 3.1[b]	< **0.01**[a]
Pennation angle (°)	15.7 ± 1.3	13.5 ± 1.2[b]	14.8 ± 1.0	**0.01**[a]

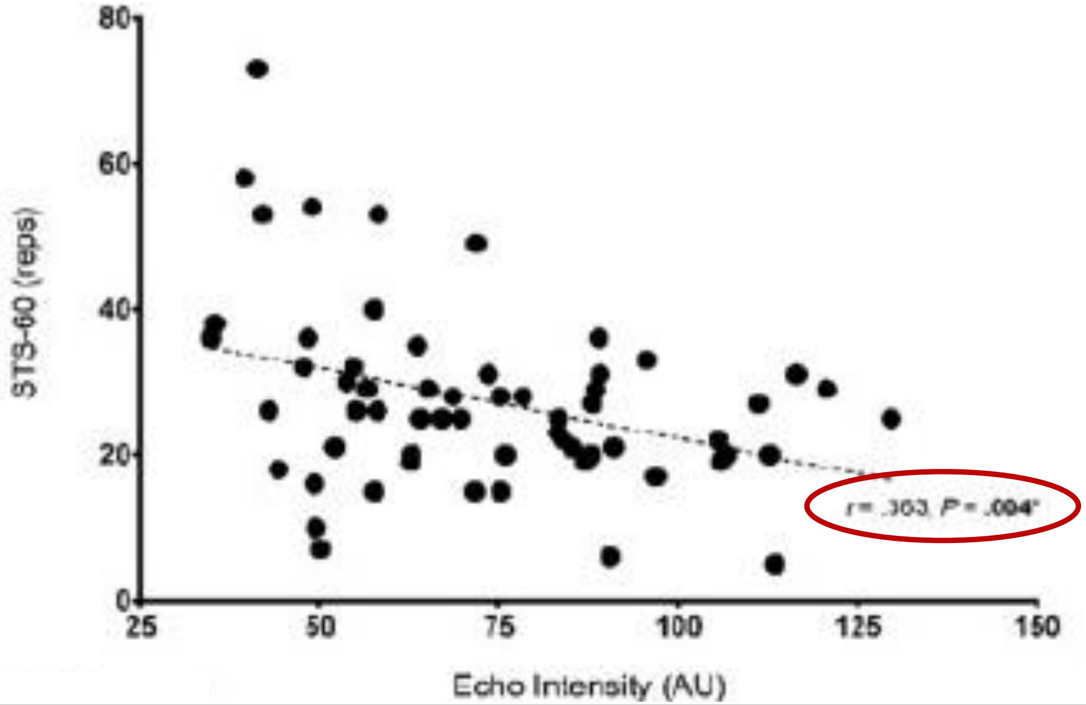
BMI: body mass index; nPCR: normalized protein catabolic rate; CC: calf circumference; HGS: handgrip strength; QT: quadriceps muscle thickness; RF-CSA: rectus femoris muscle cross-sectional area.

[a] Repeated measures ANOVA

[b] Post hoc (Bonferroni), p < 0,05 vs. T0[c].

Gonçalves T et al. Clinical Nutrition ESPEN 55 (2023) 200e207

Association of muscle echointensity with muscle function



	Unadjusted		Adjusted (Model 1)		Adjusted (Model 2)	
	β (95% CI)	P	β (95% CI)	P	β (95% CI)	P
Total cohort (all patients)						
STS-60 (repetitions)						
EI	−0.267 (−0.277 to −0.012)	0.070	−0.394 (−0.367 to −0.025)	0.026*	−0.356 (−0.351 to 0.003)	0.046*
RF-CSA	0.429 (0.866 to 4.491)	0.005*	0.421 (0.812 to 4.441)	0.006*	0.375 (0.411 to 4.266)	0.019*

Wilkinson et al. Nephrol Dial Transplant (2019) 34: 1344–1353

Lower quadriceps torque in healthy adults with worse muscle quality by echogenicity assessment

	Echogenicity[b] ≤ percentile 25th	Echogenicity > percentile 25th	p for comparisons according to echogenicity
Women			
Number of observations	20	60	
Body mass index (kg (m^2)	30.5 (28.2,31.8)[a]	29.5 (28.2,31.6)	NS
Handgrip strength (kg)	24.5 (22.5,28)	24.5 (21,26)	NS
Quadriceps torque (N)	356.5 (337,379)	327 (290.5,357)	<0.01
Men			
Number of observations	9	25	
Body mass index (kg (m^2)	30.7 (28.8,32.3)	29.9 (29.2,31.1)	NS
Handgrip strength (kg)	47 (45,50)	39 (33,45)	<0.01
Quadriceps torque (N)	567 (547,596)	511 (474,553)	0.02

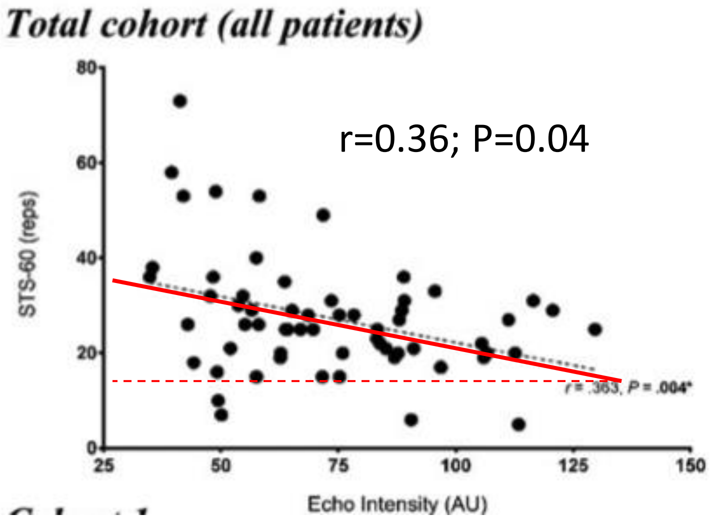
[a] = median (percentile 25th, percentile 75th).
[b] = Assessed as grayscale density of ultrasound images.

Bunout D et al. Clinical Nutrition ESPEN 55 (2023) 420e424

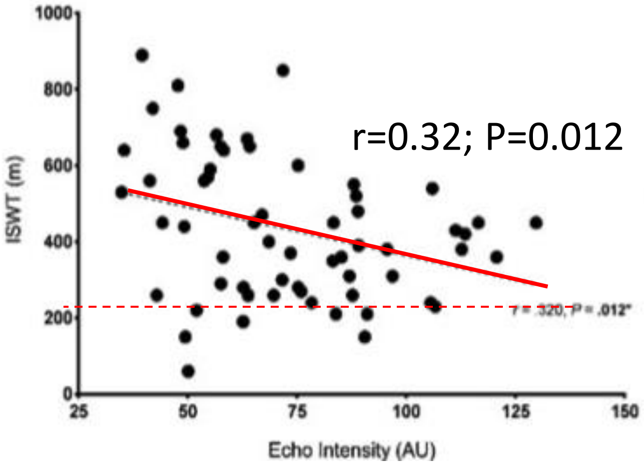
Association between Echo intensity and physical performance – Ultrasound
CKD (not on dialysis) (n=61)

55.6 ±14.2 years

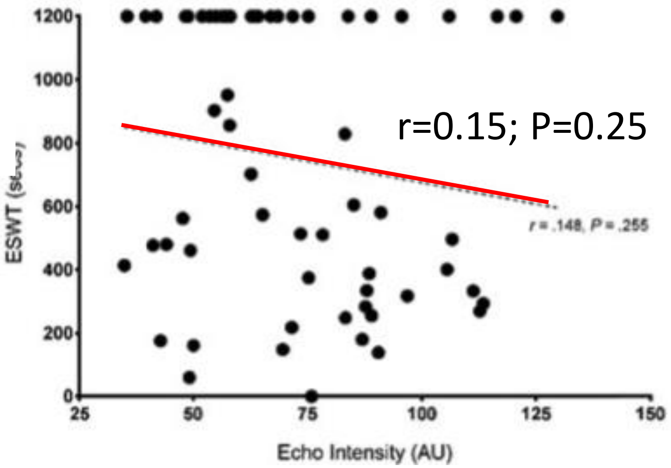
Sit-to-stand-60 second test



Incremental shuttle walk test



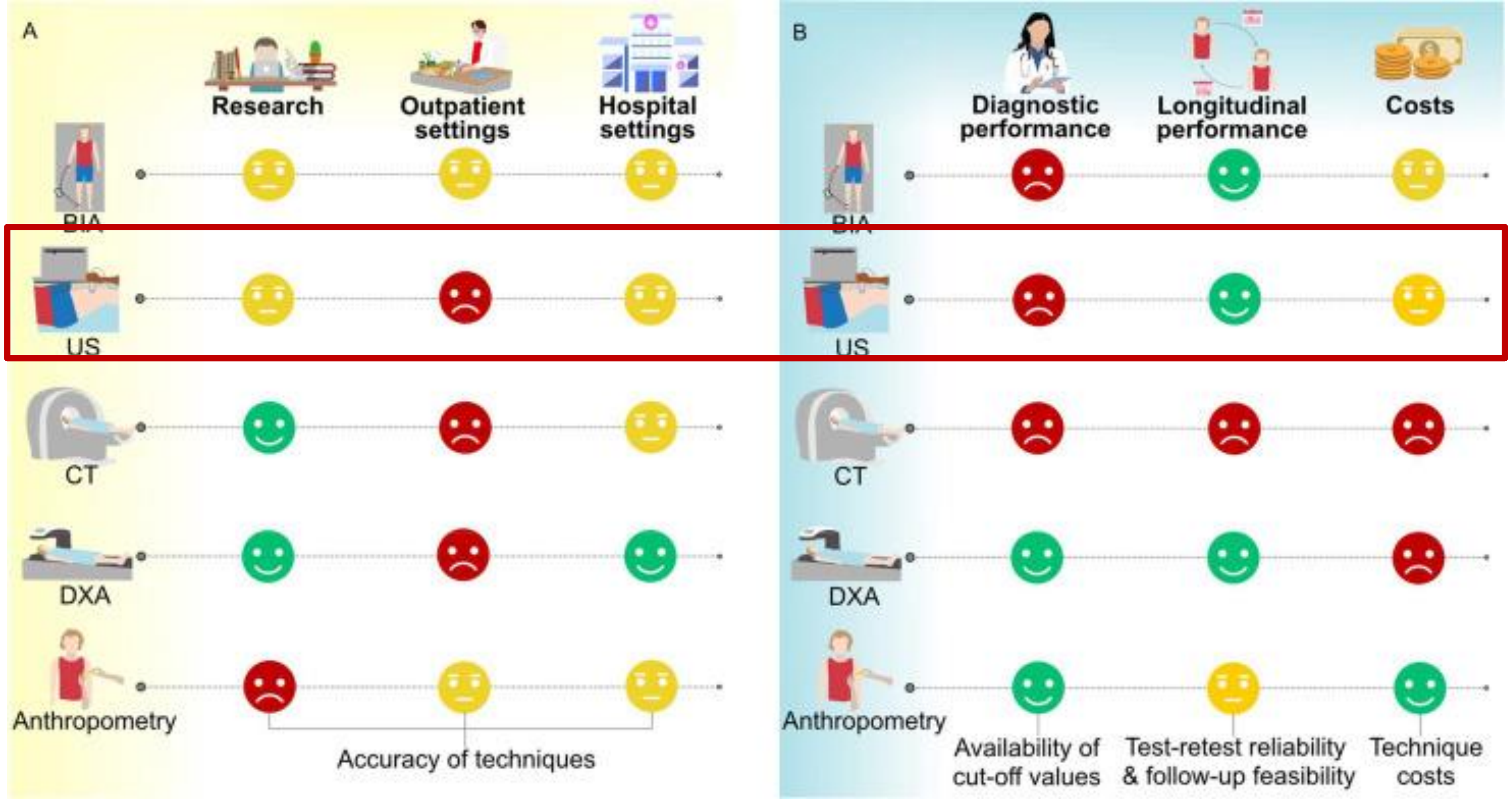
Endurance shuttle walk test



↑ Echo intensity = ↑ intramuscular fat → ↓ physical performance

Wilkinson et al, Nephrol Dial Transplant 34:1344-1353, 2019

Comparing methods



Prado C et al. Clin Nutr 2022;41(10):2244-2263. doi: 10.1016/j.clnu.2022.07.041.

Highly portable
Low cost
Easy to use

Open issues with US for clinical practice

- Diagnostic capacity: Population and sex based reference values still to be defined
- Methodological issues:
  → definition of site of scan
  → Identification of landmarks
  → patient position
  → Probe placement including angle and force applied

→ Impact accuracy of results and contribute to heterogeneity

↓

Appropriate training with validation and reliability work should be performed to ensure consistency with measurements

Summary

- Muscle abnormalities is frequent in CKD/ESKD
- Assessment of muscle quantity, quality and function are essential itens in the comprehensive nutritional assessment

	Commonly used parameters	Pros	Cons
US	Muscle size (CSA, volume) Muscle thickness Echo intensity Pennation angle	Inexpensive No radiation Portable Real time visualization of target structure Clinical application Monitoring tool Association with outcomes	Operator skills and training required Reliability and accuracy depend on operator No diagnostic capacity - lack of cut-offs

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