BJA

British Journal of Anaesthesia, 123 (1): 37–50 (2019)

doi: 10.1016/j.bja.2019.03.034
Advance Access Publication Date: 3 May 2019
Review Article

Frailty assessment: from clinical to radiological tools

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Summary

Frailty is a syndrome of cumulative decline across multiple physiological systems, which predisposes vulnerable adults to adverse events. Assessing vulnerable patients can potentially lead to interventions that improve surgical outcomes. Anaesthesiologists who care for older patients can identify frailty to improve preoperative risk stratification and subsequent perioperative planning. Numerous clinical tools to diagnose frailty exist, but none has emerged as the standard tool to be used in clinical practice. Radiological modalities, such as computed tomography and ultrasonography, are widely performed before surgery, and are therefore available to be used opportunistically to objectively evaluate surrogate markers of frailty. This review presents the importance of frailty assessment by anaesthesiologists; lists common clinical tools that have been applied; and proposes that utilising radiological imaging as an objective surrogate measure of frailty is a novel, expanding approach for which anaesthesiologists can significantly contribute to broad implementation.

Keywords: diagnostic imaging; frailty; preoperative assessment; perioperative medicine; risk assessment; sarcopenia

Ageing is accompanied by a gradual loss of reserve across multiple organ systems, which leads to an increased risk of poor health outcomes after an illness or injury.[1] Older adults experience higher rates of unplanned hospital and ICU admissions that ultimately increase all-cause mortality.[2] The biological syndrome resulting from cumulative decline across multiple physiological systems and greater vulnerability to adverse events is defined as *frailty*. Although frailty intersects with co-morbidity and disability, they are not synonymous.[3] For example, older adults with the same co-morbidities can suffer from very different levels of disability and frailty. The original definition of *frailty phenotype*, developed almost two decades ago, tests unintentional weight loss, exhaustion, muscle weakness, slowness whilst walking, and low levels of activity.[3] In most clinical tools, the identification of frailty is based on specific domains that assess physical performance, mobility, nutritional status, mental health, and cognition. Interdisciplinary experts agree that frailty is a multidimensional syndrome characterised by decreased reserve and diminished resistance to stressors; however, no single definition of frailty has been agreed upon[4] (Fig. 1).

Anaesthesiologists are increasingly recognising the potential utility of preoperative frailty assessment,[5] as frailty in older adults is associated with increased postoperative complications, including death, loss of independence, and discharge to nursing facilities after non-cardiac[6] and cardiac[7]

Editorial decision: 05 March 2019; **Accepted:** 5 March 2019

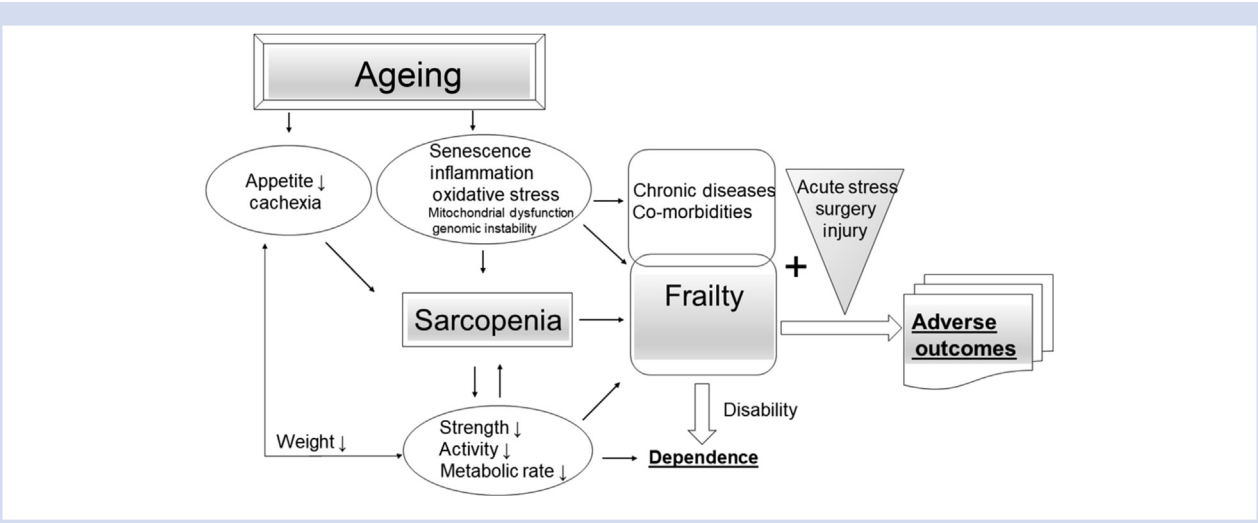

Fig 1. Conceptual model of frailty. The ageing process is associated with the activation of biological processes, such as inflammation, oxidative stress, mitochondrial dysfunction, cellular senescence, and genomic instability, which results in the development of co-morbidities, loss of muscle mass and function (sarcopenia), and frailty (a cumulative decline across multiple physiological systems). Frailty is linked to greater vulnerability to adverse outcomes especially when an acute stress (surgery or injury) is present. Sarcopenia is associated with a vicious cycle, because a reduction in strength and activity leads to loss of weight and appetite, which worsens sarcopenia. Sarcopenia is a good marker of frailty.

surgeries. However, many clinical tools to measure frailty require patient participation (e.g. grip strength, gait speed, and cognitive testing). Whilst these tasks are feasible for community-dwelling older adults, this is not the case for patients who are ill, injured, or in pain. Accordingly, in many scenarios encountered by anaesthesiologists, objective, simple markers of frailty that do not require patient participation are necessary. This review presents common frailty assessment instruments, and discusses radiological modalities that are useful and feasible for identifying frail patients in clinical situations familiar to anaesthesiologists. Opportunistic radiological studies are an objective source of surrogate markers for physical frailty. The broad implementation of available tools to better identify the frail patient will increase awareness and could improve outcomes in the perioperative and critical care setting.

Importance of frailty assessment by anaesthesiologists

Anaesthesiologists should utilise frailty assessment in a myriad of clinical settings. Whilst this will require a change in common practice, resources should be deployed in preoperative assessment clinics or health informatics to capture frailty assessments routinely in order to better assess and coordinate care for high-risk surgical patients. Recent reviews show that preoperative frailty assessment provides expanded objective, prognostic information for risk stratification[8–10] compared with the American Society of Anesthesiologists (ASA) physical status classification or the Charlson Comorbidity Index.[7] In low-risk (ASA 1–2) aged patients, preoperative frailty assessment (based on comprehensive geriatric assessment) predicted postoperative complications and increased length of stay.[11] Frailty assessment improves the consent process and assists in the formation of an individualised clinical care plan.[12] Similarly, frailty assessment on admission to the ICU is being investigated as an independent prognostic indicator.[13] Notably, the increased healthcare expenditures in frail patients have prompted some models of healthcare to incorporate payment adjustments for this population.[14]

Perioperative risk stratification

Advanced age is a risk factor for adverse surgical outcomes, but outcomes are heterogeneous and vary greatly amongst adults of similar ages.[15] Preoperative frailty in older adults is associated with poor surgical outcomes (increased morbidity, mortality, rate of complications, and poor discharge disposition) in multiple surgical fields, including cardiac surgery,[16,17] general non-cardiac surgical population,[18] oncologic surgery (colorectal cancer),[19,20] vascular surgery,[21] and orthopaedic surgery (hip fractures).[22] Regardless of the type of surgery and which assessment tool is used, the presence of frailty is associated with approximately two-to three-fold increased risk of adverse surgical outcomes.[10] The strongest association links frailty to 30 day mortality.[8] Although the American College of Surgeons and the American Geriatrics Society currently recommend preoperative evaluation of frailty in all patients aged 65 yr and older,[23] and the Society for Perioperative Assessment and Quality Improvement recommends interventions once frailty is identified,[24] there is no specific guidance on which frailty assessment instrument to use. This may contribute to the findings of a recent survey that was sent to all the members of the ASA; more than 80% of the responders answered that they 'rarely or never' assess frailty (Neuman MD, personal communication, 2018).

In-hospital risk stratification

Many healthcare encounters with older adults begin in the emergency department or the ICU setting because of acute

trauma or rapid deterioration. Older adults are often admitted to the ICU during periods of acute illness; however, only one of every four adults aged 80 yr and older will return to baseline levels of functioning 1 yr after ICU admission.[25] A recent meta-analysis that pooled the results of 10 trials of older ICU patients found that frailty is associated with increased short- and long-term mortality.[13] Surprisingly, the meta-analysis did not find that frailty is associated with increased length of stay in the ICU. The latter may reflect the influence of end-of-life palliative care and discharge practices that are often not reported. Of note, a study that assessed the duration of mechanical ventilation found no difference between frail and non-frail patients.[26] Multidimensional tools are being developed to individualise specific interventions, such as nutrition therapy, and frailty assessment is a potential tool to facilitate this type of decision-making in the ICU.[27] It is likely that frailty assessments of older patients on admission to the ICU will be useful in providing information regarding expected outcomes, but they are probably not sufficiently predictive to be of value in clinical decision-making about the withdrawal of life-sustaining treatment.[28]

Another important effect of frailty is found in *failure to rescue*, which is defined as death after a potentially treatable complication and is an important measure for surgical quality improvement initiatives.[29] After both low- and high-risk inpatient surgeries (e.g. in thoracoabdominal operations[24]), frailty is associated with failure to rescue.[30]

Perioperative interventions

Frailty assessment before surgery can inform goals-of-care discussions, as it predicts the risk of mortality and independence after surgery.[15] A striking example of the value provided by frailty assessment was demonstrated in a prospective cohort of more than 9000 adults who presented for major, elective, non-cardiac surgery. Recognition of preoperative frailty led to an administrative review (which included an anaesthesiologist) of the perioperative decision-making and surgical plan, and resulted in improved short- and long-term survival without designated changes in patient preparation.[31] As such, the idea that identifying frailty before an operation can lead to interventions that improve outcomes is appealing.

However, specific perioperative interventions aimed at perioperative 'optimisation' of frail older adults have yielded mixed results.[12] Protocols that use a geriatric 'bundle' of interventions often have difficulty with implementation and non-adherence, which lessens the impact on outcomes.[32] A trial of a comprehensive geriatric bundle in major elective abdominal surgery, with components, such as early mobilisation after surgery, oral and nutritional assistance, and orientating communication,[33] demonstrated short-term benefits that were lost after 3 months. Similarly, a multicentre prospective trial that randomised patients undergoing cancer surgery to receive an individual treatment plan after a preoperative comprehensive consultation provided positive effects at hospital discharge that were lost after 3 months.[34]

Perioperative physical training to improve postoperative functional outcomes in frail patients has been the single most commonly studied intervention. Although a long-term moderate-intensity physical activity programme in sedentary, community-dwelling older adults did not reduce the incidence of frailty,[35] the effect of physical training in the perioperative period is promising. Specifically, 6 months of supervised physical therapy and exercise training after hip fracture was superior to a low-intensity home-based programme,[36] and the addition of exercises for strength, flexibility, balance, and coordination after elective cardiac surgery was superior to aerobic exercise alone.[37] A small study that examined biweekly training session for 3–6 weeks before hip replacement found some benefit as well.[38] A bundle of preoperative interventions (pre-habilitation that includes education and exercise) before coronary bypass and valvular surgery is presently under investigation.[39]

Clinical frailty assessment tools

Comprehensive geriatric assessment is a framework for integrating clinical evaluation and intervention in vulnerable elderly patients. Comprehensive geriatric assessment can identify patients at risk of increased short-term mortality after hip fractures.[40] Preoperative geriatric evaluation before elective surgery, which initiates targeted interventions in an integrated patient management model, improves outcomes.[41,42] A screen for frailty should ideally include measures that are found in a comprehensive geriatric assessment, such as physical, emotional, and psychological domains and social support mechanisms. However, comprehensive geriatric assessment is not always feasible in the preoperative workflow, especially under acute conditions, which underscores the value of tools to measure frailty.[43] In the perioperative setting, numerous frailty assessment methods have been utilised, including observational tools, such as the Fried frailty phenotype[3] and components of the Fried phenotype[17,44–46], the Edmonton Frail Scale[47]; and the Clinical Frailty Scale.[48] The frailty index,[49,50] which identifies frailty as an accumulation of health deficits, has led to various shortened iterations sometimes referred to as the *modified frailty index*.[48,51–53] Self-reported questionnaires, such as the Fatigue, Resistance, Ambulation, Illnesses, and Loss of Weight (FRAIL) scale,[54] Tilburg Frailty Indicator,[55] Groningen Frailty Indicator,[56] Program of Research on Integration of Services for the Maintenance of Autonomy (PRISMA-7),[57] Vulnerable Elders Surgical Pathways and Outcomes Assessment (VESPA),[58] and the Risk Analysis Index,[59] require the patient to answer questions. Lastly, tools that are appropriate for databases, such as the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) tool,[60,61] or based on diagnosis codes defined by the Johns Hopkins Adjusted Clinical Groups[6] may be more appropriate for population research rather than everyday clinical use. Figure 2 summarises a few examples of observational, self-reported, and database tools that have been used in the perioperative setting. The implementation of frailty screening tools in anaesthesia practice suffers from a lack of consensus on a standard method that is relevant in different patient characteristics (e.g. we found that the elderly patients in our institution are often unable to answer questions using an electronic device) and in different types of surgeries.[8] An ideal clinical tool would also need to be easily integrated into the local preoperative workflow. Comprehensive reviews of more than 90 clinical frailty tools have been published,[43,62] but are beyond the scope of this review.

Objective surrogate markers of frailty

An objective biological measure of frailty would be a major advance in monitoring the onset of frailty and preventing its consequences.[63] Many studies have examined hormones,

Frailty tool	Type	Time to administer	Tool components	Frailty definition	Advantages	Disadvantages
Fried frailty phenotype	observational	5-10 min	Weight loss, exhaustion, weakness, gait, low physical activity.	1–2 = pre-frail, 3 or more = frail	Extensively validated, predictive of outcomes, can be extracted from a health questionnaire.	Requires special equipment and patient participation.
Frailty index	self-reported	20-30 min	Accumulated symptoms, signs, diseases, and disabilities.	A dimensionless fraction with cut-off greater than ~0.25	validated, predictive.	Requires a long time to complete.
Modified frailty index	self-reported	10-15 min	List of co-morbidities and conditions.	Similar to frailty Index.	Shorter than frailty index.	Not as reliable/ predictive as frailty index.
FRAIL scale	self-reported	5-10 min	Fatigue, resistance, ambulation, illness and loss of weight.	1–2 = pre-frail, 3 or more = frail	Simple, no training needed to administer.	Needs to be further validated.
Risk analysis index	self-reported	5-10 min	Age/cancer, co-morbidities, residence, ADLs, cognitive decline	Composite score of 0 to 81, cut-off greater than 16–21	Simple, performed by clinical staff	most questions are part of standard nursing interviews
VESPA (short form)	self-reported	10 min	Gender, ADLs, functional status, charlson comorbidity index, surgical complexity.	A dimensionless fraction with cut-off greater than ~0.25	Simple, performed by physician assistants	modest sensitivity for postoperative complications.
Edmonton frailty scale	observational/ self-reported	10-15 min	Cognition, hospitalisation, general health, independence, social support, medication, nutrition, mood, continence, timed up and go.	Composite score ≥ 8 out of 17 = frail	App available for tablet or phone.	Older adults may not be familiar or comfortable with tablet/phone.
Clinical frail scale	observational	< 5 min	Clinical descriptors and pictographs.	≥ 5 out of 9 = frail	Simple, accompanied by a visual chart.	Gestalt, unclear reliability.
ACS NSQIP	electronic health record	5-10 min	Demographics, symptoms, diseases, conditions.	Provides predicted 30 days mortality and complications	Based on very large database, highly predictive.	Limited to 30 days outcomes.

Fig 2. Commonly used clinical tools to assess frailty. Clinical modalities that are commonly used to assess frailty in the preoperative population. Tools are different in the type of data components that are collected and the definition of frailty, which leads to different time burdens to administer the tool. For a more comprehensive description, please see main article. ACS NSQIP, American College of Surgeons National Surgical Quality Improvement Program; ADL, activities of daily living; FRAIL, Fatigue, Resistance, Ambulation, Illnesses, and Loss of Weight; VESPA, Vulnerable Elders Surgical Pathways and Outcomes Assessment.

inflammatory markers, genetic variation, and the neurological and musculoskeletal systems in frailty. Numerous markers have been suggested, but none have emerged as a sufficiently robust tool to be used in routine clinical anaesthesia.

Serum markers linked to the biological basis of frailty

Underlying frailty are biological processes, such as inflammation, oxidative stress, mitochondrial dysfunction, cellular senescence, and genomic instability. This has led to a search of markers that influence or interact with these biological mechanisms. As an example, dysregulated inflammation (Inflamm-aging[64]) is one of the pillars[65] that link ageing to frailty. Pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumour necrosis factor alpha, are elevated in older adults,[66] and are associated with frailty and worse outcomes.[67] Indicators of oxidative damage to lipids and proteins are also increased in the frail.[68] Oxidative stress results in reduced response to hormones and anabolic factors that are important in cellular repair, such as insulin growth factor-1 (IGF-1).[69] IGF-1 maintains muscle mass, promotes recovery from injury, and is a sensitive marker of metabolism/nutrition.[70] Lower levels of IGF-1 are associated with frailty.[71] Frailty is also correlated with reduced expression of sirtuins,[72] a conserved family of proteins that regulate cellular metabolism. The activation of sirtuins mimics caloric restriction, which improves lifespan and health in animals.[73]

Serum markers of frailty in routine clinical practice

Several common blood tests have been evaluated as potential markers for frailty, but none are specific enough for routine use. The relationship of frailty to nutrition and inflammation may be supported by the concomitant low levels of serum albumin and high levels of C-reactive protein often found in frail patients.[74] High neutrophil and monocyte counts are associated with frailty in disabled older women, independent of IL-6 levels.[75] Higher haemoglobin in nursing home residents is correlated with reduced mortality,[76] whilst frail older subjects have lower levels of haemoglobin that are not attributable to myelosuppression or iron deficiency.[77] Vitamin B12 deficiency is associated with frailty in older women,[78] but it is uncertain if vitamin supplementation can reverse or delay frailty progression.[79] Higher serum levels of transferrin and fibrinogen (glycoproteins that are measured in the workup of anaemia and coagulation disturbances) are found in frail patients.[80]

Vitamin D insufficiency, which causes secondary elevation of parathyroid hormone, is associated with frailty in men, but not in women.[81] Low levels of cholesterol are a marker for increased mortality in the elderly[82] and correlate with frailty in older hospitalised patients.[83] Blood tests of liver function, specifically lower levels of alanine transaminase, are associated with frailty and mortality in community-dwelling men,[84] but this relationship is consistent only for the older population.[85]

Changes in body composition as surrogate markers of frailty

The ageing process is accompanied by changes in body composition with loss of skeletal muscle and lean body mass, reduced bone mineral density (osteopenia or, if more severe, osteoporosis), and increased fat mass. Although changes in mass do not necessarily reflect a similar magnitude of change in function,[86] mass and function generally move in the same direction.[87] There are numerous methods to evaluate changes in body composition. Anthropometry uses measurements obtained during clinical examination, such as BMI, skinfold thickness, and circumference of waist and extremities. Anthropometry is not precise, especially in females.[88] Bioelectrical impedance analysis is a non-invasive application of an electrical current through the body, whereby muscle mass is estimated based on the conduction of current through water (muscle is water rich); however, hydration, oedema, and nutrition status have a significant effect on the accuracy of bioelectrical impedance measurements.[89]

Sarcopenia

Determining whether frailty is attributable to sarcopenia or sarcopenia is a clinical manifestation of frailty resembles 'the chicken and the egg' question. Frailty and sarcopenia are consequences of similar pathological mechanisms that are associated with negative health-related events, and are potentially reversible.[90] *Sarcopenia* was first defined as loss of muscle tissue, which is part of the natural ageing process.[91] Later, the definition was expanded to include both low muscle mass and impaired muscle function.[92] Loss of physical function, usually measured by objective tests of gait speed and muscle strength, parallels sarcopenia[93] and is a key aspect of physical frailty. The current consensus requires the presence of both low muscle mass and reduced muscle function to meet the clinical definition and diagnostic criteria for age-related sarcopenia.[94,95] Cut-off points are specified for common tests, such as gait speed (<0.8 m s^{-1} is considered slow), grip strength by a handheld dynamometer (<26 kg for men and <16 kg for women is considered weak),[96] and lean body mass measured by whole-body dual-energy X-ray absorptiometry (DXA, previously DEXA).[97] A biochemical surrogate of sarcopenia is serum creatinine-to-serum-cystatin-C ratio, which provides an estimate of muscle mass and is associated with outcomes in the ICU.[98]

Osteopenia/osteoporosis

Osteopenia/osteoporosis and sarcopenia are concomitantly associated with frailty status in older women,[99] which may reflect common aetiologic mechanisms. Sarcopenia is associated with narrower bones and thinner cortices.[100] Lower grip strength and gait speed are independently associated with lower femoral neck bone mineral density in older men.[101] Imaging studies are recognised as the preferred tool to diagnose and evaluate osteopenia/osteoporosis.[102]

Use of radiological assessment as a surrogate marker of frailty

The association of frailty with sarcopenia and osteopenia, and the lack of feasibility in assessing muscle function in many clinical situations, has prompted the development of methods to define sarcopenia and osteopenia from existing radiological studies.[103] Many patients undergo radiological imaging before surgery, which offers a unique opportunity to measure muscle mass and osteopenia opportunistically (i.e. by analysing radiological studies that were performed for other purposes). Radiological studies can identify a change in muscle mass, but cannot provide information on muscle performance as required to make a definitive clinical diagnosis of sarcopenia.[94] We queried PubMed and Cumulative Index to Nursing and Allied Health Literature databases to identify the condition of interest (frailty, sarcopenia, or osteopenia) and a radiological method of interest (CT, MRI, ultrasound [US], or plain radiograph), using truncated keywords and Medical Subject Heading terms. Boolean expressions (e.g. AND, OR) were used to construct search queries in order to ensure comprehensive search for each criterion. No search filters or limits were used (e.g. language, article type, and study subject type [animal *vs* human]), as entries with incomplete filter tags could be inadvertently excluded from search results. During full-text review, references of interest were compared with previously identified articles.

Dual-energy X-ray absorptiometry

Dual-energy X-ray absorptiometry uses two X-ray attenuations with distinct energy peaks. One peak is absorbed mainly by lean mass (mostly muscle, which can assess sarcopenia) and the second peak by bone (used to measure bone mineral density). DXA uses a very small dose of ionising radiation; a single whole-body scan is roughly equal to background radiation received over 1 day (<10 μSv).[104] DXA is recommended to screen for osteoporosis in women older than 65 yr and older men with additional risk factors for low bone mass.[105] There are accepted reference values to detect sarcopenia by DXA (<7.26 kg m^{-2} for men; <5.45 kg m^{-2} for women[94]). However, DXA is not routinely performed to assess muscle mass or before surgery; therefore, it is not a useful tool for anaesthesiologists.

Magnetic resonance imaging

MRI is based on the observation that some atomic nuclei emit radio-frequency energy when exposed to an external magnetic field. Different timings of radio-frequency pulse sequences (T1 weighted and T2 weighted) excite the nuclear spin energy transition in the atoms, and the magnetic field gradients localise the signal. This permits the creation of very detailed resolution of tissue types, so that muscle, bone, water, or fat can be quantified precisely.[106] MRI does not involve ionising radiation, such as X-rays or CT, but it is expensive and often contraindicated in patients with certain metal objects, such as cochlear implants or cardiac pacemakers.

MRI is not performed before operation as frequently as CT and is often focused on a specific area. For example, in the evaluation for lumbar spinal stenosis (the most common indication for lumbar spinal surgery in people aged more than 65 yr), the dural sac and central canal are imaged, but the paraspinal muscles are not.[107] Despite its limitations, MRI assessment of sarcopenia is being evaluated as a prognostic marker in select groups, for example, fat-free muscle area (as a measure of muscle quality) in decompensated cirrhotic patients.[108]

Computed tomography

CT uses X-rays taken around a single axis of rotation, from different angles, to generate a computer-processed three-dimensional image. X-rays are attenuated as they pass through tissues; the attenuation is relative to air and water, and is expressed as Hounsfield units (HU) with air defined as −1000 HU and water as zero. Sarcopenia can be quantified from CT images using available (but not required) commercial software packages, such as sliceOmatic® (TomoVision, Magog, QC, Canada), MATLAB (MathWorks, Inc., Natick, MA, USA), or ImageJ (National Institutes of Health, Bethesda, MD, USA). The simplest method of quantification is to use any standard free Digital Imaging and Communications in Medicine (DICOM) compatible software to trace visually the cross-sectional area (CSA) of structures that have been correlated with frailty, such as muscle and fat. (The specifics of these cross-sectional measures will be discussed next.) A more complex method to quantify sarcopenia assigns an HU threshold from −29 to 150 HU within the traced area, which then provides the muscle mass within the area. If the traced area consists of two or more components (e.g. in fatty infiltration of the muscle myosteatosis), this method indirectly provides a measure of muscle quality.[109] A similar technique can be used to assess osteopenia/osteoporosis[110,111] by assigning HU thresholds for bone that determine specificity and sensitivity.[112] Fully automated systems that calculate body composition (e.g. muscle, bone, and fat) from abdominal or thoracic CT scans are being developed.[113] Phase contrast is a new technology that provides better soft tissue resolution.[114] Other types of CT use gamma rays (positron emission tomography and single-photon emission CT) to study muscle metabolism,[114] but these are not in routine use to assess sarcopenia.

Sarcopenia measured by CT is associated with adverse outcomes after surgery[115] and in the ICU.[116] Given their prognostic value, the opportunistic use (when the studies were performed for another purpose) of CT scans in the preoperative evaluation is relevant to anaesthesiologists.

Abdomino-pelvic CT

Abdomino-pelvic CT is routinely used in the evaluation of possible visceral injury, acute abdominal pain, or complex abdominal pathologies to determine the subsequent need for surgery. Data from CT scans are generally readily available to the anaesthesiologist. There are several anatomical structures that can assist in the identification of sarcopenia or osteopenia, which can then identify patients at risk for adverse outcomes.

Skeletal muscle index sarcopenia

Skeletal muscle index is determined by measuring the total muscle CSA at the level of the third lumber vertebra (L3) (in cm^2) and dividing it by the patient's height (in m^2), which normalises CSA to stature. Measuring skeletal muscle index can be facilitated by image processing software packages. At the L3 level, several muscles are identified: psoas, *erector spinae*, *quadratus lumborum*, *transversus abdominis*, external and internal obliques, and *rectus abdominis*. To determine the skeletal muscle index, all muscles within a single slice are identified using HU-based tissue-specific thresholds for muscle (the most common HU range is −29 to +150) that exclude fatty infiltration.[117] Whilst diagnostic thresholds using CT-based measurements are not described in the sarcopenia consensus guidelines, a linear correlation exists between muscle area measured in a single lumbar CT image and DXA-measured whole-body fat-free mass and appendicular skeletal muscle.[118] In patients who had both DXA and CT imaging, the corresponding thresholds for skeletal muscle index for sarcopenia (extrapolated from DXA) are <55.4 cm^2 m^{-2} in men and <38.9 cm^2 m^{-2} in women.[119] A study that defined sarcopenia by stratifying for optimal prediction of mortality in patients with solid tumours of the respiratory or gastrointestinal tract found very similar values (<52.4 cm^2 m^{-2} in men and <38.5 cm^2 m^{-2} in women).[117] Low skeletal muscle index in patients undergoing colorectal cancer resection is associated with an increased rate of post-operative infection and delayed recovery.[120] In patients undergoing transcatheter aortic valve replacement, every 14 cm^2 m^{-2} increase in skeletal muscle index was associated with a 1 day reduction in length of stay.[121] Low skeletal muscle index in mechanically ventilated ICU patients is associated with increased mortality at hospital discharge,[122] 30 days,[123] and 6 months,[109] and with 1 yr mortality in older trauma patients in the ICU.[116]

Psoas muscle sarcopenia

The psoas muscle is the main flexor of the hip, and provides postural support of the lumbar spine, sacroiliac, and hip joints. The use of a single muscle has been criticised for not being representative of whole-body sarcopenia,[124] but is well suited for clinical use in anaesthesia. Typically, psoas CSA (after tracing the circumference of the muscles in the axial plane) reflects the sum of both psoas muscle areas rather than that of a single unilateral muscle. The association of low psoas muscle density or low psoas muscle volume with adverse surgical outcomes has been described.[125] Psoas muscle sarcopenia is associated with an increased risk of complications after resection of hepatic liver metastasis,[126] but not in older patients undergoing simple lumbar spine surgery, in which the psoas muscle may be an inappropriate surrogate because of its anatomical connection to spine function.[127] Psoas muscle sarcopenia in older trauma patients is associated with mortality at 6 months[128] and 2 yr[129] after discharge from the hospital.

Vertebral body osteopenia/osteoporosis

Image analysis procedures typically entail vertebral body identification via sagittal cross reference and use of the axial slice in the middle of the vertebral body. A small region of interest of the lumbar vertebral body trabecular bone is encircled, and the average HU within that bone is calculated. The use of the first lumbar vertebra is common, but other lumbar vertebrae have been used with excellent intra-class correlation of average density.[130] Useful thresholds for osteoporosis using L1 average density are dependent on the goal of the threshold. For example, a threshold of ≤160 HU was 90% sensitive, and a threshold of ≤110 HU was >90% specific.[112] We and others have demonstrated that older injured patients with sarcopenia and osteoporosis suffer from higher morbidity[131] and mortality[116] than those with sarcopenia, osteoporosis, or neither (Fig. 3).

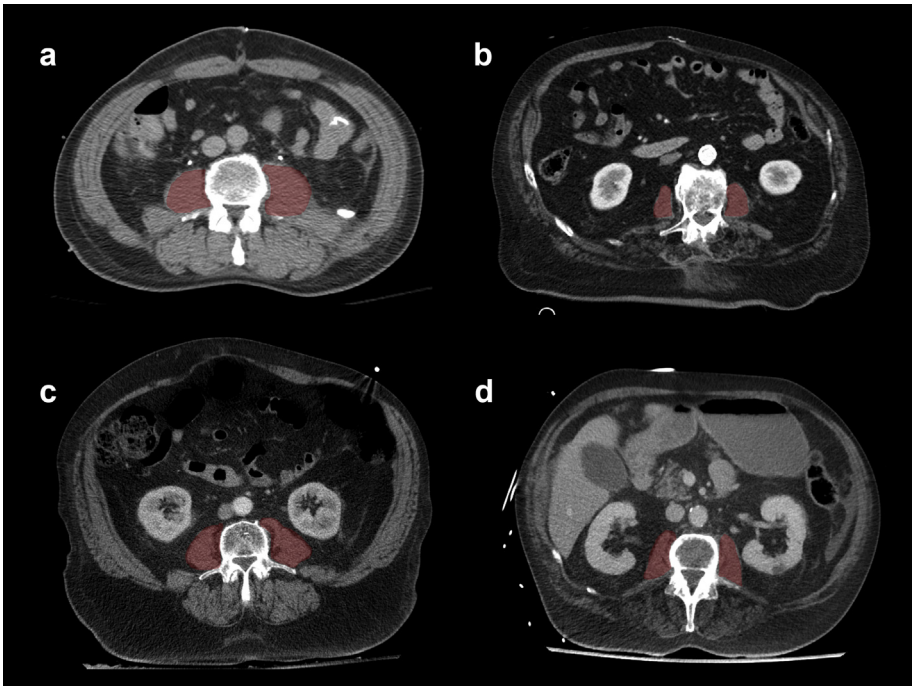

Fig 3. Psoas sarcopenia and vertebral osteopenia in a single CT image at L3 level. A single image from abdomino-pelvic CT can be used to assess sarcopenia and osteopenia at the L3 level by assessing for psoas muscle cross-sectional area (CSA) as a marker of sarcopenia and vertebral bone density as a marker of osteopenia. (a) Normal psoas CSA and bone density, (b) sarcopenia with normal bone density, (c) normal psoas CSA with osteopenia, and (d) sarcopenia and osteopenia. The psoas muscle is coloured in red.

Thoracic CT

Thoracic CTs are commonly obtained before chest surgery during preoperative cancer staging and workup of major trauma, or to diagnose pulmonary embolus. Consequently, many ICU and surgical patients will have thoracic imaging data that can be easily assessed by the anaesthesiologist. Similar tools to assess sarcopenia and osteopenia are used in thoracic CT as in abdomino-pelvic CT. CT scans are quantified

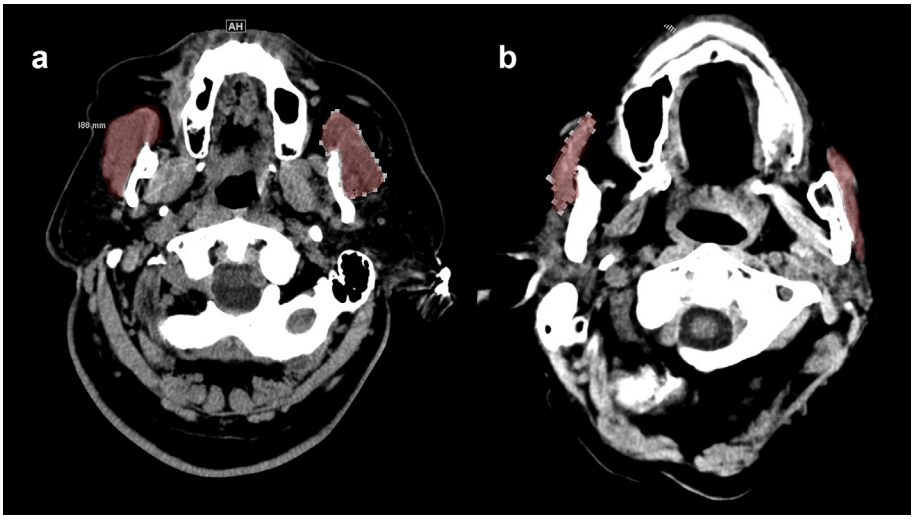

Fig 4. CT assessment of masseter muscle sarcopenia. The masseter muscle is the main muscle of mastication and can be identified (coloured in red) in cranial Computed tomography (CT), using horizontal images 1 cm caudad to the zygomatic bones. (a) Normal masseter cross-sectional area and (b) masseter muscle sarcopenia.

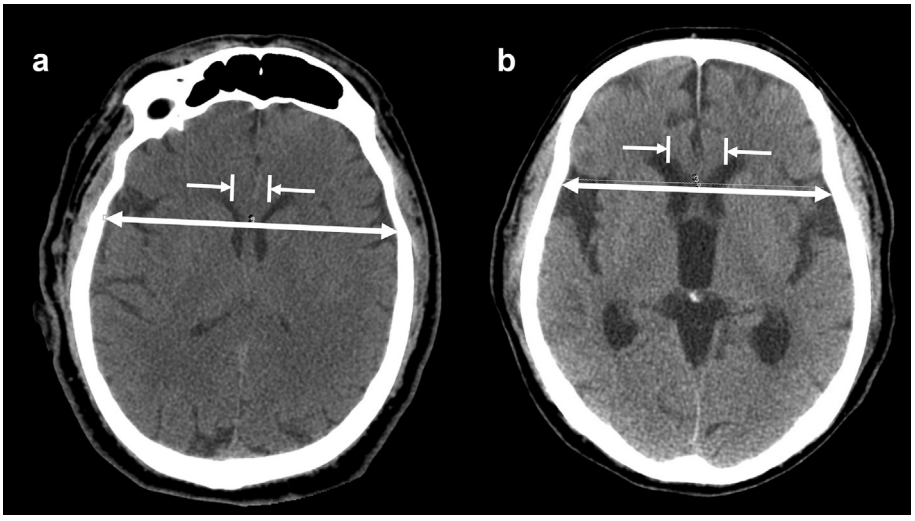

Fig 5. Cranial CT assessment of brain atrophy index. The brain atrophy index is measured by the ratio of the width of two lateral ventricles at the head of the caudate nucleus (also described at the intercaudate distance, denoted by two vertical lines between inward pointing arrows) to the width of the skull (denoted by outward pointing arrows). Measurements are taken at the cranial-caudal level of the fornix. (a) Normal brain atrophy index and (b) increased brain atrophy index.

in a similar method used for abdominal skeletal mass index. Specifically, thoracic muscle CSA calculated from a single axial CT slice at the level of the carina is well correlated with thoracic muscle volume.[132] An average of three slices (one at the carina level, and second and third slices [1–1.25 mm] above and below [which contain the *pectoralis major* and *minor*, intercostals, *serratus anterior*, paraspinal, and *latissimus dorsi*]) provides an even stronger correlation.[133] Single-muscle sarcopenia of the *pectoralis* muscle[134] and the *erector spinae* muscles,[135] as measured by thoracic CT, can provide prognostic information in patients with chronic obstructive pulmonary disease.

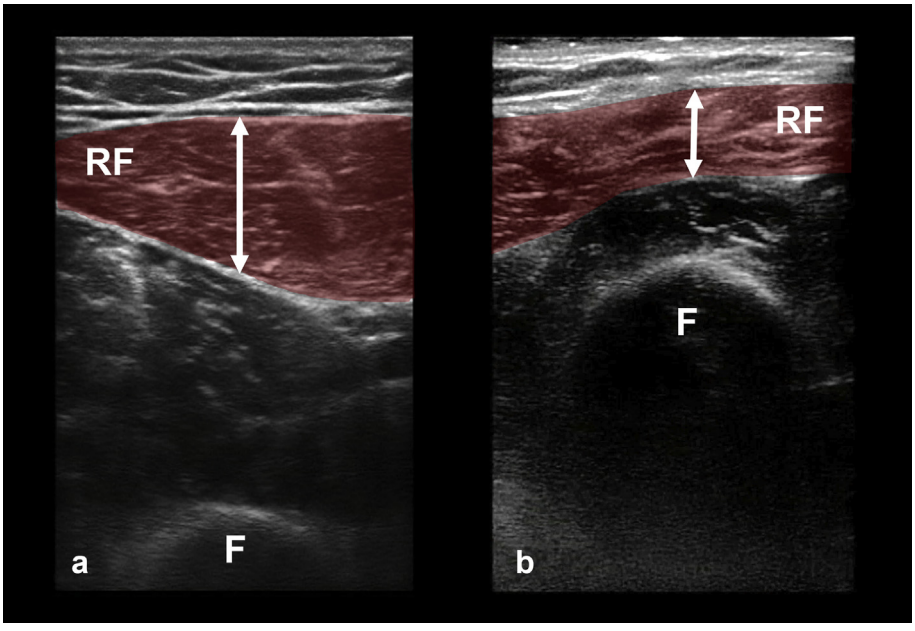

Fig 6. Ultrasound (US) assessment of *rectus femoris* (RF) muscle sarcopenia. A two-dimensional US image using a probe placed in transverse orientation at the level of the mid-anterior thigh. The RF muscle is coloured in red. The caliper measures the width of the muscle at the anterior/posterior plane of the middle of the femur (F). (a) Normal muscle mass and (b) sarcopenia.

Cranial CT

Cranial imaging is obtained in the aged even after a minor head injury,[136] and can provide an assessment of sarcopenia and a potential indirect marker of cognitive decline secondary to brain atrophy.[137] Sarcopenia can be assessed by CSA of the temporalis[138] and the masseter[129] muscle (Fig. 4). Lower masseter muscle CSA measured by cranial CT is associated with increased mortality in injured older adults.[129,139] The brain atrophy index, the ratio of the width of two lateral ventricles at the head of the caudate nucleus (or the intercaudate distance) to the width of the skull at the cranial-caudal level of the fornix, is increased as a result of secondary frontal horn ventricular enlargement that reflects atrophy of deep frontal subcortical white matter[140] (Fig. 5). Our group investigated the use of cranial CT to determine the outcomes in injured older adults, and found that long-term mortality is higher in those with masseter muscle sarcopenia and a high brain atrophy index (Tanabe and colleagues, JAMA Surgery, May 8, 2019).

Ultrasoography

Ultrasoography has become a core competency for anaesthesiologists and is included in the Accreditation Council for Graduate Medical Education (ACGME) Anesthesiology Program Requirements. US is a safe, inexpensive, portable, and radiation-free imaging modality; the low intensity used for diagnostic imaging does not usually cause heat or pressure.[141] Numerous studies have evaluated the use of US to detect sarcopenia with promising results.[142] Muscle thickness measures are obtained using onscreen calipers, measuring the distance between the upper margin of the underlying bone and the lower boundary of the ventral fascia of the muscle group of interest. A comprehensive assessment, performed whilst the patient stands, utilises anterior and posterior muscle groups, and is well correlated to total body muscle mass.[143] Comprehensive protocols often assess muscle mass in numerous sites (e.g. a nine-site protocol [forearm, biceps, triceps, abdomen, subscapularis, quadriceps, hamstrings, gastrocnemius, and tibialis anterior]). This protocol is probably impractical in the acute care setting and has led to the development of a bedside, four-site protocol, with the patient supine. In this method, a transverse approach is used to examine the bilateral anterior muscle thickness of *rectus femoris* and *vastus intermedius* muscles at the midpoint of the femur, and two-thirds the distance between the anterior superior iliac spine and the upper pole of the patella.[144] A single point of measurement has been described that focuses on the mid-anterior thigh, half the distance between the lateral condyle of the femur and the greater trochanter[143] (Fig. 6).

Numerous studies have evaluated the use of US to detect sarcopenia with promising results.[142] Although no standard clinical assessment exists, using US to identify fat,[145] bone,[146] and muscle[147] has been described. Sarcopenia as assessed by US is well correlated to clinical frailty in the older outpatient population.[148] In surgical ICU patients, sarcopenia diagnosed by US measurement of *rectus femoris* CSA is associated with discharge to nursing facility or in-hospital mortality.[149]

Conclusions, applications, and future direction

Frailty is a major problem in the perioperative period. Frailty assessment by anaesthetists identifies those who are most vulnerable to adverse outcomes, and provides an opportunity to improve perioperative and hospital outcomes. Whilst there is no consensus on the best way to evaluate patients, numerous tools have been validated. The scores generated from many of these tools are reliable for predicting frailty and are highly associated with patient outcomes. Although a 'silver bullet' to treat frailty has not been identified, once frailty is recognised, numerous management decisions and interventions can be launched to raise awareness of the vulnerabilities of the frail patient and to optimise the allocation of resources. Despite the value of frailty assessment, it has not gained wide implementation by anaesthesiologists.

Radiological imaging modalities, both opportunistic and as part of a screening test, provide objective and quantitative tools to detect surrogate markers of frailty. Imaging is currently an area of intense investigation to bridge the gap between clinical assessments and objective markers of frailty, and anaesthesiologists are uniquely trained to become leaders in this endeavour. Anaesthesiologists routinely use health technology in an innovative fashion, and their role as perioperative and critical care physicians can be leveraged to make significant advances in the field of frailty detection. For example, expertise in US can be used longitudinally to objectively assess a patient over time. Anaesthesiologists who evaluate patients before surgery should participate in developing pattern recognition software that will automatically identify preoperative radiological markers of frailty in CT and MRI studies. Anaesthesiologists have a long history of spearheading efforts to advance patient safety. Implementation of frailty assessments in the older patient represents a timely opportunity for anaesthesia leadership in the perioperative and critical care setting.

Authors' contributions

Conceptual framework: IB.
Literature search: IB, SK.
Writing first draft: IB.
Conceptual figure and table design: IB, TNP, MJR.
Radiological figure design/analysis: SK.
Manuscript editing/proofing: all authors.
Reviewing/approving final draft: all authors.

Declaration of interest

The authors declare that they have no conflicts of interest.

References

1. Robertson DA, Savva GM, Kenny RA. Frailty and cognitive impairment—a review of the evidence and causal mechanisms. *Ageing Res Rev* 2013; **12**: 840–51
2. Wen Y-C, Chen L-K, Hsiao F-Y. Predicting mortality and hospitalization of older adults by the multimorbidity frailty index. *PLoS One* 2017; **12**, e0187825
3. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001; **56**: M146–57
4. Rodríguez-Mañas L, Féart C, Mann G, et al. Searching for an operational definition of frailty: a Delphi method based consensus statement. The frailty operative definition-consensus conference project. *J Gerontol A Biol Sci Med Sci* 2013; **68**: 62–7

5. Amrock LG, Deiner S. The implication of frailty on preoperative risk assessment. *Curr Opin Anaesthesiol* 2014; **27**: 330–5
6. McIsaac DI, Bryson GL, van Walraven C. Association of frailty and 1-year postoperative mortality following major elective noncardiac surgery: a population-based cohort study. *JAMA Surg* 2016; **151**: 538–45
7. Lee DH, Buth KJ, Martin B-J, Yip AM, Hirsch GM. Frail patients are at increased risk for mortality and prolonged institutional care after cardiac surgery. *Circulation* 2010; **121**: 973–8
8. Lin H-S, Watts JN, Peel NM, Hubbard RE. Frailty and postoperative outcomes in older surgical patients: a systematic review. *BMC Geriatr* 2016; **16**: 157
9. Oakland K, Nadler R, Cresswell L, Jackson D, Coughlin PA. Systematic review and meta-analysis of the association between frailty and outcome in surgical patients. *Ann R Coll Surg Engl* 2016; **98**: 80–5
10. Beggs T, Sepehri A, Szwajcer A, Tangri N, Arora RC. Frailty and perioperative outcomes: a narrative review. *Can J Anaesth* 2015; **62**: 143–57
11. Choi JY, Yoon SJ, Kim SW, et al. Prediction of postoperative complications using multidimensional frailty score in older female cancer patients with American Society of Anesthesiologists physical status class 1 or 2. *J Am Coll Surg* 2015; **221**: 652–60. e2
12. McIsaac DI, Jen T, Mookerji N, Patel A, Lalu MM. Interventions to improve the outcomes of frail people having surgery: a systematic review. *PLoS One* 2017; **12**, e0190071
13. Muscedere J, Waters B, Varambally A, et al. The impact of frailty on intensive care unit outcomes: a systematic review and meta-analysis. *Intensive Care Med* 2017; **43**: 1105–22
14. Kautter J, Ingber M, Pope GC. Medicare risk adjustment for the frail elderly. *Health Care Financ Rev* 2008; **30**: 83–93
15. Oresanya LB, Lyons WL, Finlayson E. Preoperative assessment of the older patient: a narrative review. *JAMA* 2014; **311**: 2110–20
16. Sundermann S, Dademasch A, Praetorius J, et al. Comprehensive assessment of frailty for elderly high-risk patients undergoing cardiac surgery. *Eur J Cardiothorac Surg* 2011; **39**: 33–7
17. Green P, Arnold SV, Cohen DJ, et al. Relation of frailty to outcomes after transcatheter aortic valve replacement (from the PARTNER trial). *Am J Cardiol* 2015; **116**: 264–9
18. Hewitt J, Moug SJ, Middleton M, et al. Prevalence of frailty and its association with mortality in general surgery. *Am J Surg* 2015; **209**: 254–9
19. Neuman HB, Weiss JM, Leverson G, et al. Predictors of short-term postoperative survival after elective colectomy in colon cancer patients $\geq$ 80 years of age. *Ann Surg Oncol* 2013; **20**: 1427–35
20. Tan KY, Kawamura YJ, Tokomitsu A, Tang T. Assessment for frailty is useful for predicting morbidity in elderly patients undergoing colorectal cancer resection whose comorbidities are already optimized. *Am J Surg* 2012; **204**: 139–43
21. Ambler GK, Brooks DE, Al Zuhir N, et al. Effect of frailty on short- and mid-term outcomes in vascular surgical patients. *Br J Surg* 2015; **102**: 638–45
22. Krishnan M, Beck S, Havelock W, Eeles E, Hubbard RE, Johansen A. Predicting outcome after hip fracture: using a frailty index to integrate comprehensive geriatric assessment results. *Age Ageing* 2014; **43**: 122–6
23. Chow WB, Rosenthal RA, Merkow RP, et al. Optimal preoperative assessment of the geriatric surgical patient: a best practices guideline from the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society. *J Am Coll Surg* 2012; **215**: 453–66
24. Mosquera C, Bermudez JM, Evans JL, Spaniolas K, MacGillivary DC, Fitzgerald TL. Frailty predicts failure to rescue after thoracoabdominal operation. *J Am Coll Surg* 2018; **226**: 978–86
25. Heyland DK, Garland A, Bagshaw SM, et al. Recovery after critical illness in patients aged 80 years or older: a multi-center prospective observational cohort study. *Intensive Care Med* 2015; **41**: 1911–20
26. Le Maguet P, Roquilly A, Lasocki S, et al. Prevalence and impact of frailty on mortality in elderly ICU patients: a prospective, multicenter, observational study. *Intensive Care Med* 2014; **40**: 674–82
27. Heyland DK, Dhaliwal R, Jiang X, Day AG. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. *Crit Care* 2011; **15**: R268
28. Hogan DB, Maxwell CJ, Afilalo J, et al. A scoping review of frailty and acute care in middle-aged and older individuals with recommendations for future research. *Can Geriatr J* 2017; **20**: 22–37
29. Ghaferi AA, Birkmeyer JD, Dimick JB. Complications, failure to rescue, and mortality with major inpatient surgery in medicare patients. *Ann Surg* 2009; **250**: 1029–34
30. Shah R, Attwood K, Arya S, et al. Association of frailty with failure to rescue after low-risk and high-risk inpatient surgery. *JAMA Surg* 2018; **153**, e180214
31. Hall DE, Arya S, Schmid KK, et al. Association of a frailty screening initiative with postoperative survival at 30, 180, and 365 days. *JAMA Surg* 2017; **152**: 233–40
32. Bakker FC, Persoon A, Bredie SJ, et al. The CareWell in Hospital program to improve the quality of care for frail elderly inpatients: results of a before-after study with focus on surgical patients. *Am J Surg* 2014; **208**: 735–46
33. Chen CC, Chen CN, Lai IR, Huang GH, Saczynski JS, Inouye SK. Effects of a modified Hospital Elder Life Program on frailty in individuals undergoing major elective abdominal surgery. *J Am Geriatr Soc* 2014; **62**: 261–8
34. Hempenius L, Slaets JP, van Asselt D, de Bock TH, Wiggers T, van Leeuwen BL. Long term outcomes of a geriatric liaison intervention in frail elderly cancer patients. *PLoS One* 2016; **11**, e0143364
35. Trombetti A, Hars M, Hsu FC, et al. Effect of physical activity on frailty: secondary analysis of a randomized controlled trial. *Ann Intern Med* 2018; **168**: 309–16
36. Binder EF, Brown M, Sinacore DR, Steger-May K, Yarasheski KE, Schechtman KB. Effects of extended outpatient rehabilitation after hip fracture: a randomized controlled trial. *JAMA* 2004; **292**: 837–46
37. Molino-Lova R, Pasquini G, Vannetti F, et al. Effects of a structured physical activity intervention on measures of physical performance in frail elderly patients after cardiac rehabilitation: a pilot study with 1-year follow-up. *Intern Emerg Med* 2013; **8**: 581–9

38. Hoogeboom TJ, Dronkers JJ, van den Ende CH, Oosting E, van Meeteren NL. Preoperative therapeutic exercise in frail elderly scheduled for total hip replacement: a randomized pilot trial. *Clin Rehabil* 2010; **24**: 901–10
39. Stammers AN, Kehler DS, Afilalo J, et al. Protocol for the PREHAB study—pre-operative Rehabilitation for reduction of Hospitalization after coronary Bypass and valvular surgery: a randomised controlled trial. *BMJ Open* 2015; **5**, e007250
40. Palmer A, Taitsman LA, Reed MJ, Nair BG, Bentov I. Utility of geriatric assessment in the projection of early mortality following hip fracture in the elderly patients. *Geriatr Orthop Surg Rehabil* 2018; **9**. 2151459318813976
41. Harari D, Hopper A, Dhesi J, Babic-Illman G, Lockwood L, Martin F. Proactive care of older people undergoing surgery ('POPS'): designing, embedding, evaluating and funding a comprehensive geriatric assessment service for older elective surgical patients. *Age Ageing* 2007; **36**: 190–6
42. Eamer G, Taheri A, Chen SS, et al. Comprehensive geriatric assessment for older people admitted to a surgical service. *Cochrane Database Syst Rev* 2018; **1**: CD012485
43. Dent E, Kowal P, Hoogendijk EO. Frailty measurement in research and clinical practice: a review. *Eur J Intern Med* 2016; **31**: 3–10
44. Kristjansson SR, Rønning B, Hurria A, *et al*. A comparison of two pre-operative frailty measures in older surgical cancer patients. J Geriatr Oncol 3: 2012, 1–7.
45. Ensrud KE, Ewing SK, Taylor BC, et al. Frailty and risk of falls, fracture, and mortality in older women: the study of osteoporotic fractures. *J Gerontol A Biol Sci Med Sci* 2007; **62**: 744–51
46. Afilalo J, Eisenberg MJ, Morin J-F, et al. Gait speed as an incremental predictor of mortality and major morbidity in elderly patients undergoing cardiac surgery. *J Am Coll Cardiol* 2010; **56**: 1668–76
47. Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton frail scale. *Age Ageing* 2006; **35**: 526–9
48. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005; **173**: 489–95
49. Rockwood K, Mitnitski A. Frailty in relation to the accumulation of deficits. *J Gerontol A Biol Sci Med Sci* 2007; **62**: 722–7
50. Mitnitski AB, Mogilner AJ, MacKnight C, Rockwood K. The mortality rate as a function of accumulated deficits in a frailty index. *Mech Ageing Dev* 2002; **123**: 1457–60
51. Farhat JS, Velanovich V, Falvo AJ, et al. Are the frail destined to fail? Frailty index as predictor of surgical morbidity and mortality in the elderly. *J Trauma Acute Care Surg* 2012; **72**: 1526–31
52. Karam J, Tsiouris A, Shepard A, Velanovich V, Rubinfeld I. Simplified frailty index to predict adverse outcomes and mortality in vascular surgery patients. *Ann Vasc Surg* 2013; **27**: 904–8
53. Tsiouris A, Hammoud ZT, Velanovich V, Hodari A, Borgi J, Rubinfeld I. A modified frailty index to assess morbidity and mortality after lobectomy. *J Surg Res* 2013; **183**: 40–6
54. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. *J Nutr Health Aging* 2012; **16**: 601–8
55. Gobbens RJJ, van Assen MALM, Luijkx KG, Wijnen-Sponselee MT, Schols JMGA. The Tilburg frailty indicator: psychometric properties. J Am Med Dir Assoc 11, 2010, 344–355.
56. Peters LL, Boter H, Buskens E, Slaets JPJ. Measurement properties of the Groningen Frailty Indicator in home-dwelling and institutionalized elderly people. J Am Med Dir Assoc 13, 2012, 546–551.
57. Raîche M, Hébert R, Dubois M-F. PRISMA-7: a case-finding tool to identify older adults with moderate to severe disabilities. *Arch Gerontol Geriatr* 2008; **47**: 9–18
58. Min L, Hall K, Finlayson E, et al. Estimating risk of postsurgical general and geriatric complications using the VESPA Preoperative Tool. *JAMA Surg* 2017; **152**: 1126–33
59. Hall DE, Arya S, Schmid KK, et al. Development and initial validation of the risk analysis index for measuring frailty in surgical populations. *JAMA Surg* 2017; **152**: 175–82
60. Velanovich V, Antoine H, Swartz A, Peters D, Rubinfeld I. Accumulating deficits model of frailty and postoperative mortality and morbidity: its application to a national database. *J Surg Res* 2013; **183**: 104–10
61. Seib CD, Rochefort H, Chomsky-Higgins K, et al. Association of patient frailty with increased morbidity after common ambulatory general surgery operations. *JAMA Surg* 2018; **153**: 160–8
62. Robinson TN, Walston JD, Brummel NE, et al. Frailty for surgeons: review of a National Institute on Aging Conference on Frailty for Specialists. *J Am Coll Surg* 2015; **221**: 1083–92
63. Viña J, Tarazona-Santabalbina FJ, Pérez-Ros P, et al. Biology of frailty: modulation of ageing genes and its importance to prevent age-associated loss of function. *Mol Aspects Med* 2016; **50**: 88–108
64. Franceschi C, Bonafe M, Valensin S, et al. Inflamm-aging. An evolutionary perspective on immunosenescence. *Ann N Y Acad Sci* 2000; **908**: 244–54
65. Kennedy BK, Berger SL, Brunet A, et al. Geroscience: linking aging to chronic disease. *Cell* 2014; **159**: 709–13
66. Michaud M, Balardy L, Moulis G, et al. Proinflammatory cytokines, aging, and age-related diseases. *J Am Med Dir Assoc* 2013; **14**: 877–82
67. Giovannini S, Onder G, Liperoti R, et al. Interleukin-6, C-reactive protein, and tumor necrosis factor-alpha as predictors of mortality in frail, community-living elderly individuals. *J Am Geriatr Soc* 2011; **59**: 1679–85
68. Ingles M, Gambini J, Carnicero JA, et al. Oxidative stress is related to frailty, not to age or sex, in a geriatric population: lipid and protein oxidation as biomarkers of frailty. *J Am Geriatr Soc* 2014; **62**: 1324–8
69. O'Connor JC, McCusker RH, Strle K, Johnson RW, Dantzer R, Kelley KW. Regulation of IGF-I function by proinflammatory cytokines: at the interface of immunology and endocrinology. *Cell Immunol* 2008; **252**: 91–110
70. Werner H, Weinstein D, Bentov I. Similarities and differences between insulin and IGF-I: structures, receptors, and signalling pathways. *Arch Physiol Biochem* 2008; **114**: 17–22
71. Doi T, Makizako H, Tsutsumimoto K, et al. Association between insulin-like growth factor-1 and frailty among older adults. *J Nutr Health Aging* 2018; **22**: 68–72
72. Kumar R, Mohan N, Upadhyay AD, et al. Identification of serum sirtuins as novel noninvasive protein markers for frailty. *Aging Cell* 2014; **13**: 975–80

73. Dali-Youcef N, Lagouge M, Froelich S, Koehl C, Schoonjans K, Auwerx J. Sirtuins: the 'magnificent seven', function, metabolism and longevity. *Ann Med* 2007; **39**: 335–45
74. Hubbard RE, O'Mahony MS, Calver BL, Woodhouse KW. Nutrition, inflammation, and leptin levels in aging and frailty. *J Am Geriatr Soc* 2008; **56**: 279–84
75. Leng SX, Xue Q-L, Tian J, Huang Y, Yeh S-H, Fried LP. Associations of neutrophil and monocyte counts with frailty in community-dwelling disabled older women: results from the Women's Health and Aging Studies I. *Exp Gerontol* 2009; **44**: 511–6
76. Landi F, Russo A, Danese P, et al. Anemia status, hemoglobin concentration, and mortality in nursing home older residents. *J Am Med Dir Assoc* 2007; **8**: 322–7
77. Leng S, Chaves P, Koenig K, Walston J. Serum interleukin-6 and hemoglobin as physiological correlates in the geriatric syndrome of frailty: a pilot study. *J Am Geriatr Soc* 2002; **50**: 1268–71
78. Matteini AM, Walston JD, Fallin MD, et al. Markers of B-vitamin deficiency and frailty in older women. *J Nutr Health Aging* 2008; **12**: 303–8
79. O'Leary F, Samman S. Vitamin B(12) in health and disease. *Nutrients* 2010; **2**: 299–316
80. Darvin K, Randolph A, Ovalles S, et al. Plasma protein biomarkers of the geriatric syndrome of frailty. *J Gerontol A Biol Sci Med Sci* 2014; **69**: 182–6
81. Shardell M, Hicks GE, Miller RR, et al. Association of low vitamin D levels with the frailty syndrome in men and women. *J Gerontol A Biol Sci Med Sci* 2009; **64**: 69–75
82. Schatz IJ, Masaki K, Yano K, Chen R, Rodriguez BL, Curb JD. Cholesterol and all-cause mortality in elderly people from the Honolulu Heart Program: a cohort study. *Lancet* 2001; **358**: 351–5
83. Ranieri P, Rozzini R, Franzoni S, Barbisoni P, Trabucchi M. Serum cholesterol levels as a measure of frailty in elderly patients. *Exp Aging Res* 1998; **24**: 169–79
84. Le Couteur DG, Blyth FM, Creasey HM, et al. The association of alanine transaminase with aging, frailty, and mortality. *J Gerontol A Biol Sci Med Sci* 2010; **65**: 712–7
85. Liu Z, Ning H, Que S, Wang L, Qin X, Peng T. Complex association between alanine aminotransferase activity and mortality in general population: a systematic review and meta-analysis of prospective studies. *PLoS One* 2014; **9**, e91410
86. Goodpaster BH, Park SW, Harris TB, et al. The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. *J Gerontol A Biol Sci Med Sci* 2006; **61**: 1059–64
87. Keller K, Engelhardt M. Strength and muscle mass loss with aging process. Age and strength loss. *Muscles Ligaments Tendons J* 2013; **3**: 346–50
88. Al-Gindan YY, Hankey C, Govan L, Gallagher D, Heymsfield SB, Lean ME. Derivation and validation of simple equations to predict total muscle mass from simple anthropometric and demographic data. *Am J Clin Nutr* 2014; **100**: 1041–51
89. Heber D, Ingles S, Ashley JM, Maxwell MH, Lyons RF, Elashoff RM. Clinical detection of sarcopenic obesity by bioelectrical impedance analysis. *Am J Clin Nutr* 1996; **64**. 472S–7S
90. Cesari M, Landi F, Vellas B, Bernabei R, Marzetti E. Sarcopenia and physical frailty: two sides of the same coin. *Front Aging Neurosci* 2014; **6**: 192
91. Rosenberg IH. Sarcopenia: origins and clinical relevance. *J Nutr* 1997; **127**. 990S –1S
92. Morley JE, Baumgartner RN, Roubenoff R, Mayer J, Nair KS. *Sarcopenia J Lab Clin Med* 2001; **137**: 231–43
93. Bauer JM, Sieber CC. Sarcopenia and frailty: a clinician's controversial point of view. *Exp Gerontol* 2008; **43**: 674–8
94. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European working group on sarcopenia in older people. *Age Ageing* 2010; **39**: 412–23
95. Cruz-Jentoft AJ, Landi F, Schneider SM, et al. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). *Age Ageing* 2014; **43**: 748–59
96. Alley DE, Shardell MD, Peters KW, et al. Grip strength cutpoints for the identification of clinically relevant weakness. *J Gerontol A Biol Sci Med Sci* 2014; **69**: 559–66
97. Cawthon PM, Peters KW, Shardell MD, et al. Cutpoints for low appendicular lean mass that identify older adults with clinically significant weakness. *J Gerontol A Biol Sci Med Sci* 2014; **69**: 567–75
98. Kashani KB, Frazee EN, Kukralova L, et al. Evaluating muscle mass by using markers of kidney function: development of the sarcopenia index. *Crit Care Med* 2017; **45**: e23–9
99. Frisoli A, Chaves PH, Ingham SJM, Fried LP. Severe osteopenia and osteoporosis, sarcopenia, and frailty status in community-dwelling older women: results from the Women's Health and Aging Study (WHAS) II. *Bone* 2011; **48**: 952–7
100. Szulc P, Beck TJ, Marchand F, Delmas PD. Low skeletal muscle mass is associated with poor structural parameters of bone and impaired balance in elderly men—the MINOS study. *J Bone Miner Res* 2005; **20**: 721–9
101. Kenny AM, Waynik IY, Smith J, Fortinsky R, Kleppinger A, McGee D. Association between level of frailty and bone mineral density in community-dwelling men. *J Clin Densitom* 2006; **9**: 309–14
102. Link TM. Osteoporosis imaging: state of the art and advanced imaging. *Radiology* 2012; **263**: 3–17
103. Boutin RD, Yao L, Canter RJ, Lenchik L. Sarcopenia: current concepts and imaging implications. *AJR Am J Roentgenol* 2015; **205**: W255–66
104. Shepherd JA, Ng BK, Sommer MJ, Heymsfield SB. Body composition by DXA. *Bone* 2017; **104**: 101–5
105. Schousboe JT, Shepherd JA, Bilezikian JP, Baim S. Executive summary of the 2013 international society for clinical densitometry position development conference on bone densitometry. *J Clin Densitom* 2013; **16**: 455–66
106. Mitsiopoulos N, Baumgartner RN, Heymsfield SB, Lyons W, Gallagher D, Ross R. Cadaver validation of skeletal muscle measurement by magnetic resonance imaging and computerized tomography. *J Appl Physiol* 1998; **85**: 115–22. 1985
107. Kuittinen P, Sipola P, Leinonen V, et al. Preoperative MRI findings predict two-year postoperative clinical outcome in lumbar spinal stenosis. *PLoS One* 2014; **9**, e106404
108. Praktiknjo M, Book M, Luetkens J, et al. Fat-free muscle mass in magnetic resonance imaging predicts acute-on-chronic liver failure and survival in decompensated cirrhosis. *Hepatology* 2017; **67**: 1014–26
109. Looijaard WG, Dekker IM, Stapel SN, et al. Skeletal muscle quality as assessed by CT-derived skeletal

muscle density is associated with 6-month mortality in mechanically ventilated critically ill patients. *Crit Care* 2016; **20**: 386
110. Lang TF, Keyak JH, Heitz MW, et al. Volumetric quantitative computed tomography of the proximal femur: precision and relation to bone strength. *Bone* 1997; **21**: 101–8
111. Pickhardt PJ, Lee LJ, del Rio AM, et al. Simultaneous screening for osteoporosis at CT colonography: bone mineral density assessment using MDCT attenuation techniques compared with the DXA reference standard. *J Bone Miner Res* 2011; **26**: 2194–203
112. Pickhardt PJ, Pooler BD, Lauder T, del Rio AM, Bruce RJ, Binkley N. Opportunistic screening for osteoporosis using abdominal computed tomography scans obtained for other indications. *Ann Intern Med* 2013; **158**: 588–95
113. Popuri K, Cobzas D, Esfandiari N, Baracos V, Jagersand M. Body composition assessment in axial CT images using FEM-based automatic segmentation of skeletal muscle. *IEEE Trans Med Imaging* 2016; **35**: 512–20
114. Shimada H. Imaging of glucose uptake during walking in elderly adults. *Curr Aging Sci* 2012; **5**: 51–7
115. Reisinger KW, van Vugt JL, Tegels JJ, et al. Functional compromise reflected by sarcopenia, frailty, and nutritional depletion predicts adverse postoperative outcome after colorectal cancer surgery. *Ann Surg* 2015; **261**: 345–52
116. Kaplan SJ, Pham TN, Arbabi S, et al. Association of radiologic indicators of frailty with 1-year mortality in older trauma patients: opportunistic screening for sarcopenia and osteopenia. *JAMA Surg* 2017; **152**, e164604
117. Prado CM, Lieffers JR, McCargar LJ, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. *Lancet Oncol* 2008; **9**: 629–35
118. Shen W, Punyanitya M, Wang Z, et al. Total body skeletal muscle and adipose tissue volumes: estimation from a single abdominal cross-sectional image. *J Appl Physiol* 2004; **97**: 2333–8. 1985
119. Mourtzakis M, Prado CMM, Lieffers JR, Reiman T, McCargar LJ, Baracos VE. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. *Appl Physiol Nutr Metab* 2008; **33**: 997–1006
120. Lieffers JR, Bathe OF, Fassbender K, Winget M, Baracos VE. Sarcopenia is associated with postoperative infection and delayed recovery from colorectal cancer resection surgery. *Br J Cancer* 2012; **107**: 931–6
121. Dahya V, Xiao J, Prado CM, et al. Computed tomography-derived skeletal muscle index: a novel predictor of frailty and hospital length of stay after transcatheter aortic valve replacement. *Am Heart J* 2016; **182**: 21–7
122. Moisey LL, Mourtzakis M, Cotton BA, et al. Skeletal muscle predicts ventilator-free days, ICU-free days, and mortality in elderly ICU patients. *Crit Care* 2013; **17**: R206
123. Fuchs G, Thevathasan T, Chretien YR, *et al*. Lumbar skeletal muscle index derived from routine computed tomography exams predict adverse post-extubation outcomes in critically ill patients. J Crit Care 44, 2018, 117–123.
124. Rutten IJG, Ubachs J, Kruitwagen RFPM, Beets-Tan RGH, Olde Damink SWM, Van Gorp T. Psoas muscle area is not representative of total skeletal muscle area in the assessment of sarcopenia in ovarian cancer. *J Cachexia Sarcopenia Muscle* 2017; **8**: 630–8
125. Amini N, Spolverato G, Gupta R, et al. Impact total psoas volume on short- and long-term outcomes in patients undergoing curative resection for pancreatic adenocarcinoma: a new tool to assess sarcopenia. *J Gastrointest Surg* 2015; **19**: 1593–602
126. Peng PD, van Vledder MG, Tsai S, et al. Sarcopenia negatively impacts short-term outcomes in patients undergoing hepatic resection for colorectal liver metastasis. *HPB (Oxford)* 2011; **13**: 439–46
127. Charest-Morin R, Street J, Zhang H, et al. Frailty and sarcopenia do not predict adverse events in an elderly population undergoing non-complex primary elective surgery for degenerative conditions of the lumbar spine. *Spine J* 2017; **18**: 245–54
128. Leeper CM, Lin E, Hoffman M, et al. Computed tomography abbreviated assessment of sarcopenia following trauma: the CAAST measurement predicts 6-month mortality in older adult trauma patients. *J Trauma Acute Care Surg* 2016; **80**: 805–11
129. Wallace JD, Calvo RY, Lewis PR, et al. Sarcopenia as a predictor of mortality in elderly blunt trauma patients: comparing the masseter to the psoas using computed tomography. *J Trauma Acute Care Surg* 2017; **82**: 65–72
130. Romme EA, Murchison JT, Phang KF, et al. Bone attenuation on routine chest CT correlates with bone mineral density on DXA in patients with COPD. *J Bone Miner Res* 2012; **27**: 2338–43
131. Ebbeling L, Grabo DJ, Shashaty M, et al. Psoas:lumbar vertebra index: central sarcopenia independently predicts morbidity in elderly trauma patients. *Eur J Trauma Emerg Surg* 2014; **40**: 57–65
132. Singer LG, Chowdhury NA, Faughnan ME, et al. Effects of recipient age and diagnosis on health-related quality-of-life benefit of lung transplantation. *Am J Respir Crit Care Med* 2015; **192**: 965–73
133. Rozenberg D, Mathur S, Herridge M, et al. Thoracic muscle cross-sectional area is associated with hospital length of stay post lung transplantation: a retrospective cohort study. *Transpl Int* 2017; **30**: 713–24
134. McDonald ML, Diaz AA, Ross JC, et al. Quantitative computed tomography measures of pectoralis muscle area and disease severity in chronic obstructive pulmonary disease. A cross-sectional study. *Ann Am Thorac Soc* 2014; **11**: 326–34
135. Tanimura K, Sato S, Fuseya Y, et al. Quantitative assessment of erector spinae muscles in patients with chronic obstructive pulmonary disease. Novel chest computed tomography-derived index for prognosis. *Ann Am Thorac Soc* 2016; **13**: 334–41
136. Haydel MJ, Preston CA, Mills TJ, Luber S, Blaudeau E, DeBlieux PM. Indications for computed tomography in patients with minor head injury. *N Engl J Med* 2000; **343**: 100–5
137. Gallucci M, Piovesan C, Di Battista ME. Associations between the frailty index and brain atrophy: the treviso dementia (TREDEM) registry. *J Alzheimers Dis* 2018; **62**: 1623–34
138. Ranganathan K, Terjimanian M, Lisiecki J, et al. Temporalis muscle morphomics: the psoas of the craniofacial skeleton. *J Surg Res* 2014; **186**: 246–52
139. Hu P, Uhlich R, White J, Kerby J, Bosarge P. Sarcopenia measured using masseter area predicts early mortality

following severe traumatic brain injury. *J Neurotrauma* 2018; **35**: 2400–6
140. Bermel RA, Bakshi R, Tjoa C, Puli SR, Jacobs L. Bicaudate ratio as a magnetic resonance imaging marker of brain atrophy in multiple sclerosis. *Arch Neurol* 2002; **59**: 275–80
141. Nelson TR, Fowlkes JB, Abramowicz JS, Church CC. Ultrasound biosafety considerations for the practicing sonographer and sonologist. *J Ultrasound Med* 2009; **28**: 139–50
142. Ticinesi A, Meschi T, Narici MV, Lauretani F, Maggio M. Muscle ultrasound and sarcopenia in older individuals: a clinical perspective. *J Am Med Dir Assoc* 2017; **18**: 290–300
143. Abe T, Kondo M, Kawakami Y, Fukunaga T. Prediction equations for body composition of Japanese adults by B-mode ultrasound. *Am J Hum Biol* 1994; **6**: 161–70
144. Gruther W, Benesch T, Zorn C, et al. Muscle wasting in intensive care patients: ultrasound observation of the M. quadriceps femoris muscle layer. *J Rehabil Med* 2008; **40**: 185–9
145. Wagner DR. Ultrasound as a tool to assess body fat. *J Obes* 2013; **2013**: 280713
146. Karjalainen J, Riekkinen O, Toyras J, Kroger H, Jurvelin J. Ultrasonic assessment of cortical bone thickness in vitro and in vivo. *IEEE Trans Ultrason Ferroelectr Freq Control* 2008; **55**: 2191–7
147. Mayans D, Cartwright MS, Walker FO. Neuromuscular ultrasonography: quantifying muscle and nerve measurements. *Phys Med Rehabil Clin N Am* 2012; **23**: 133–48 [xii]
148. Mirón Mombiela R, Facal de Castro F, Moreno P, Borras C. Ultrasonic echo intensity as a new noninvasive in vivo biomarker of frailty. *J Am Geriatr Soc* 2017; **65**: 2685–90
149. Mueller N, Murthy S, Tainter CR, et al. Can sarcopenia quantified by ultrasound of the rectus femoris muscle predict adverse outcome of surgical intensive care unit patients and frailty? A prospective, observational cohort study. *Ann Surg* 2016; **264**: 1116–24

Handling editor: J.G. Hardman