

## REVIEW

# Frailty in the older surgical patient: a review

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## Abstract

The rate of surgical procedures in the older population is rising. Despite surgical, anaesthetic and medical advances, older surgical patients continue to suffer from adverse postoperative outcomes. Comorbidities and reduction in physiological reserve are consistently identified as major predictors of poor postoperative outcome in this population. Frailty can be defined as a lack of physiological reserve seen across multiple organ systems and is an independent predictor of mortality, morbidity and institutionalisation after surgery. Despite this identification of frailty as a significant predictor of adverse postoperative outcome, there is not yet a consensus on the definition of frailty or how best to assess and diagnose it. This review describes our current definitions of frailty and discusses the available methods of assessing frailty, the impact on the older surgical population and the emerging potential for modification of this important syndrome.

**Keywords:** *frailty, surgery, older adults, outcomes, interventions, elderly*

## Introduction

### Ageing of the surgical population

Over the last 20 years, the number of older people undergoing surgical procedures has increased faster than the rate of population ageing [1, 2]. This is likely to be related to changes in anaesthetic and surgical techniques, patient expectations and increasing evidence of improved morbidity and mortality following surgery even in the oldest old [3–6]. However, despite surgical and anaesthetic advances and improvements in the medical care of older surgical patients, adverse postoperative outcomes, particularly medical complications still remain commoner in older people when compared with their younger counterparts [7–11]. These complications are particularly significant as 30-day postoperative complications are more important than preoperative risk factors and intraoperative factors in determining survival after major surgery [7, 11]. There has been a focus on age and pre-existing comorbidities as the main predictors of adverse postoperative outcome in the older surgical population [7, 9, 12]. The role of frailty as an independent risk factor for adverse postoperative outcomes is now emerging [13, 14].

### Why measure frailty in surgical patients?

Studies in various surgical populations have identified frailty as an independent risk factor for major morbidity, mortality, protracted length of stay (LOS) and institutional discharge [13–17]. Its importance is being recognised in influential reports such as the most recent National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report, 'An Age Old Problem' [18]. The authors of this report stated in the second of their principle recommendations that 'comorbidity, disability and frailty need to be clearly recognised as independent markers of risk in the elderly' [18]. Within the older surgical population the process of preoperative assessment provides an opportunity for proactive recognition of the frailty syndrome. The preoperative assessment process can be considered to serve two broad purposes. First, to risk stratify patients in order that health professionals, patients and their relatives or carers are fully informed of the inherent risks in undergoing a procedure. Second, in order that modifiable factors are proactively identified and optimised preoperatively, thus improving the patient's likelihood of a successful outcome.

The appeal of measuring frailty in a surgical population lies in its utility both as a tool for preoperative risk

stratification and also as a method for identifying potentially modifiable factors that can be optimised preoperatively.

### Defining frailty

Frailty has been a concept in the clinical and research literature for two decades now. While most geriatricians can accurately identify a frail patient, a consensus regarding the definition has proved difficult to achieve [19–21]. This may stem from the need to encompass a complex and poorly understood syndrome in terms that are useful both to the clinician and to the researcher. In addition an overlap exists between frailty and other syndromes or issues seen commonly in an older person [22]. These include sarcopenia, cachexia, disability and comorbidity [23, 24]. The debate continues about whether frailty is a syndrome or a series of age-related risk factors predicting the likelihood of future adverse events [19, 25].

Broadly speaking, frailty can be thought of as a decreased physiological reserve across multiple organ systems [26]. Campbell defines frailty as ‘a condition or syndrome which results from a multi-system reduction in reserve capacity to the extent that a number of physiological systems are close to, or past, the threshold of symptomatic clinical failure. As a consequence the frail person is at increased risk of disability and death from minor external stresses’ [27]. The debate continues about the position frailty occupies on the spectrum between normal ageing at one end, and discreet pathophysiological entity at the other [19].

### Models of frailty

Two main models of frailty exist: the frailty phenotype [28] and the frailty index or deficit accumulation model [29–32]. These models were derived from data taken from the Cardiovascular Health Study and the Canadian Study of Health and Aging, respectively [31, 33].

#### Frailty phenotype

The frailty phenotype proposes the relationship between a set of criteria that define frailty (unintentional weight loss, grip strength, self-reported exhaustion, gait speed, low physical activity level) and the effect on certain outcome measures (new falls, deteriorating mobility, disability, hospitalisation, death) [28].

#### Deficit accumulation model of frailty

The deficit accumulation model of frailty reflects the number of deficits an individual has accrued across a number of different domains [29, 30, 34]. These domains include current illnesses, ability to manage activities of daily living (ADL) and physical signs. This model allows for the calculation of a ‘frailty index’ which can be thought of as ‘a count of an individual’s accumulated deficits’ [30, 34, 35].

The debate continues as to whether cognitive impairment, socio-demographic measures and affective disorders should be included in the definition of frailty. Furthermore, there is no consensus on whether frailty should be a clinical diagnosis or based on a combination of medical, functional and laboratory measures.

### Measuring frailty

The lack of consensus on which method should be used to measure frailty is due to several issues [36]. First, the absence of a universally accepted definition hampers precise identification or measurement. Second, there are different intentions in measuring frailty; assessing, screening, case-finding or predicting prognosis. Third, measurement tools differ according to whether the tool is intended for the researcher, lay research assistant, geriatrician, general practitioner, public health physician, epidemiologist or allied health professional [25, 37]. Fourth, measurement of frailty has mainly been undertaken in the research setting and thus the assessment of clinically feasible tools is only just emerging in the literature.

#### Which tools do we have?

The measurement tools that exist are either scoring systems based on various aspects of physical, cognitive or functional capability [28, 30, 38–40] or are ‘surrogate single measures’ of frailty based on assessment of functional status [41–43]. These purely functional measures include forearm grip strength and gait speed. The majority of available tools have not been assessed according to their clinometric properties. A systematic review of frailty measurement tools recently concluded that while there are clearly advantages and disadvantages of all measurement tools, the most suitable tool for frailty research is the frailty index [30, 40].

#### Which tool to use clinically?

The question of the best clinical tool for assessment of frailty remains unanswered. Choosing a frailty assessment tool for the older surgical population should be undertaken in light of the two main purposes of preoperative identification of frailty: risk stratification and identification of factors for potential modification. For example, single surrogate measures such as grip strength have the benefit of simplicity, reproducibility and application to the busy preoperative setting and can define an individual as being ‘at risk’ of adverse postoperative outcomes [44]. Such measures do not point the clinician to clear areas for modification of frailty though. In contrast the Edmonton Frail Scale (EFS) or Reported Edmonton Frail Scale (REFS, in which the timed up and go assessment has been replaced by reported physical functioning) can also effectively risk stratify but may better highlight aspects of frailty that are amenable to preoperative optimisation [13, 38, 45]. These may include

preoperative medication review, treatment of depression, cognitive screening or pre-emptive provision of social support. The EFS has been validated for use among non-geriatricians and assesses multiple domains in less than 5 min [38]. At the opposite end of the spectrum the Comprehensive Assessment of Frailty (CAF) score, developed according to the Fried criteria to assess frailty in the context of cardiac surgery, is complex and cardiac specific (including measures such as brain natriuretic peptide level and ejection fraction) [15]. While this may be useful in the research setting, it is difficult to see how measures such as this could be easily applied in a clinical context.

American studies have used variables associated with frailty, rather than a specific validated frailty score [46, 47]. This method is not in keeping with the current emphasis on accurately defining frailty and other complex geriatric syndromes (such as sarcopenia) [20, 23, 25]. Furthermore, unless an accepted definition or assessment method is used in such studies, the applicability of the findings may be limited.

## Frailty and surgery

### Prevalence of frailty in the older surgical population

The prevalence of frailty in patients of all ages presenting for surgical procedures is quoted at between 4.1 and 50.3% [14–17]. This wide variation relates to the issues of definition, measurement and varying populations studied. A recent UK study used the Fried model to define frailty in community-dwelling people aged between 65 and 74 years [48]. Prevalence rates of frailty in this study were 8.5% for women and 4.1% for men. Studies examining older patients undergoing elective cardiac and non-cardiac surgery quote prevalence rates of frailty at between 41.8 and 50.3% [14–16]. This high prevalence of frailty in older surgical populations, compared with the prevalence rate of less than 10% observed in older community-dwelling individuals, highlights the vulnerability of this patient group.

### Impact of frailty on surgical outcomes

Table 1 summarises the impact of frailty across different surgical populations. The table illustrates the relative paucity of research and the disparate approach to the measurement of frailty.

Notably the two studies by Robinson *et al.* (Table 1) show a very high incidence of post-discharge institutionalisation (26 and 30%, respectively) [46, 47]. While the high rate of institutionalisation may reflect a difference in the American social care model, the findings of these studies raise two questions. First, was it appropriate to perform surgery in this group with over a quarter subsequently needing institutional care? Second, what is the role for intervention targeted at individual components of the frailty syndrome in improving surgical outcomes?

## Inflammatory biomarkers and postoperative outcomes

A recent study examined inflammatory biomarkers, thought to be important in the pathophysiology of frailty, and the association with postoperative complications in older colorectal surgical patients [49]. Patients aged 70 years or over were defined as frail, pre-frail or robust using comprehensive geriatric assessment (CGA) and an approximation to the frailty phenotype. The inflammatory biomarkers C-reactive protein (CRP), interleukin-6 (IL-6), tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ) and D-dimer were examined 2 weeks prior to elective resection for colorectal cancer. Levels of CRP, IL-6 and TNF- $\alpha$  increased significantly with increasing frailty level. Having adjusted for tumour location, which is an established risk factor for postoperative complications, both CGA defined frailty and IL-6 were predictive of complications.

## Can the syndrome of frailty be modified?

### The interaction of frailty with other geriatric syndromes

Figure 1 shows the overlap between frailty and other geriatric syndromes.

The aetiology of these conditions is incompletely understood but involves some common processes [23, 50–53]. Certainly the dysregulation of inflammatory pathways seems to be important in the pathophysiology of frailty [54]. Several biomarkers and combinations of biomarkers have been suggested as measures of frailty. These include CRP, albumin, IL-6 and TNF- $\alpha$  [52, 55, 56]. This overlap in the pathophysiology of geriatric syndromes may be relevant in the development of future modifications.

### Progression of the frailty syndrome

Transition from one frailty state to another has a resultant impact upon mortality [57]. The natural history of frailty shows that it is more common to progress to a state of greater frailty than to improve to a state of lesser frailty [57]. However, even without intervention, some individuals become ‘less frail’. These observed transitions between different ‘degrees of frailty’ suggest that potential interventions aimed at lessening the state of frailty may well be effective.

### Using exercise to modify frailty

Spontaneous increase in gait speed over a 12-month period in community-dwelling over 65 year olds predicted an improved 8-year survival [58]. This raises the question of whether targeted interventions to improve gait speed would have similar effects reducing frailty and improving mortality and outcomes after surgery. Individual and group exercise programmes have been shown to improve mobility and ADL in the long-term care population many of whom are frail [59]. Contradictory evidence exists regarding the role

Table 1.

Method of measuring frailty	Impact of frailty on surgical outcome	Surgical population studied	Authors and reference
Grip strength	Increased postoperative complications Increased LOS	All ages Elective major abdominal surgery	Klidjian <i>et al.</i> [44]
Gait speed	Composite endpoint of in-hospital postoperative mortality or major morbidity (as defined by Society of Thoracic Surgeons criteria)	≥70 years old	Afilalo <i>et al.</i> [16]
Edmonton Frail Scale	Cardiac surgery Postoperative complications Prolonged LOS Increased institutionalisation rate	≥70 years old Lower limb orthopaedic surgery Spinal surgery Abdominal surgery Vascular surgery	Dasgupta <i>et al.</i> [13]
Frailty score based on frailty phenotype	Postoperative complications Prolonged LOS New institutionalisation at discharge	≥65 years old Elective surgery (major and minor)	Makary <i>et al.</i> [14]
Comprehensive Assessment of Frailty Score	Increase in 30-day mortality	Cardiac surgery	Sundermann <i>et al.</i> [15]
8 'markers' of frailty (age, cognition, recent weight loss, BMI, serum albumin, falls, depression, haematocrit)	Increase in 6-month mortality (although underpowered for this) Post-discharge institutionalisation	≥65 years old General, thoracic, urology and vascular surgery (patients undergoing major elective surgery necessitating postoperative surgical ICU admission)	Robinson <i>et al.</i> [46]
14 frailty 'characteristics' in 6 domains (comorbidity, function, cognition, geriatric syndromes, extrinsic frailty) NB: most closely associated were TUAG ≥ 15 seconds and functional dependence	Institutionalisation at hospital discharge	≥ 65 years old Elective general, cardiac, thoracic, urology and vascular surgery (patients undergoing major elective surgery necessitating postoperative surgical ICU admission)	Robinson <i>et al.</i> [47]
Frailty defined as any impairment in activities of daily living (Katz index) or impairment of ambulation or diagnosis of dementia	In-hospital mortality Institutional discharge Mid-term survival	All ages Cardiac surgery	Lee <i>et al.</i> [17]
Groningen frailty indicator	Post-operative delirium	All ages Elective vascular surgery	Pol <i>et al.</i> [86]

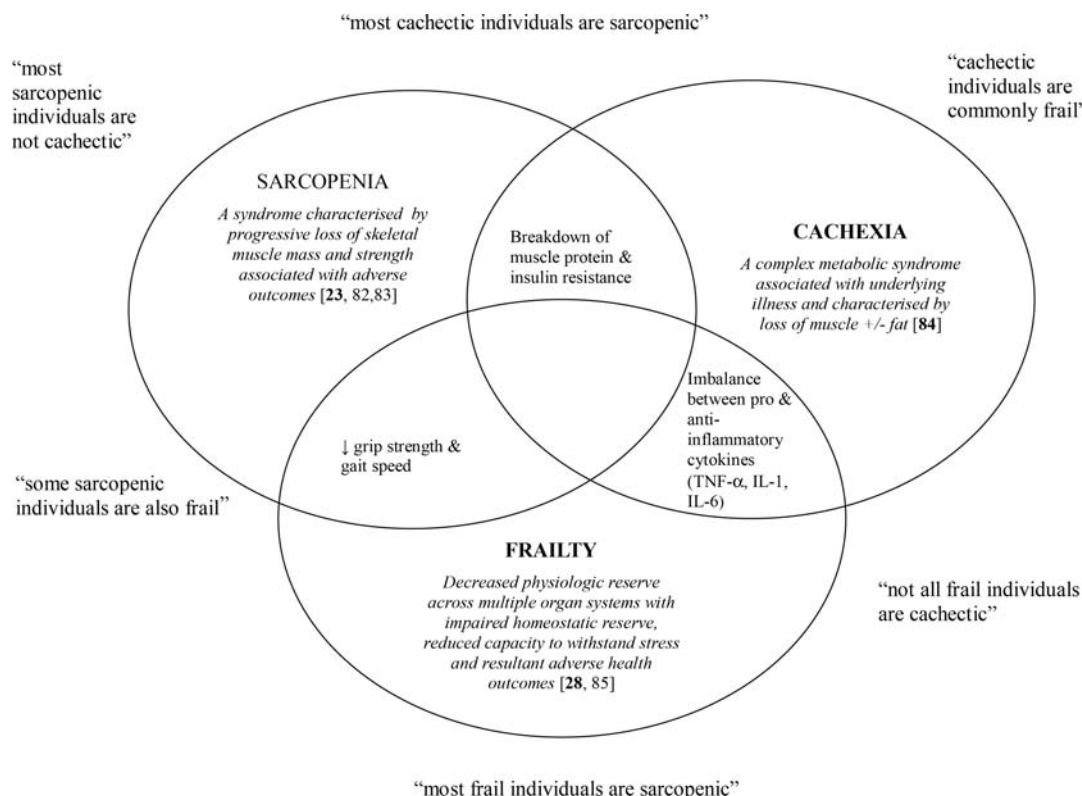
of different forms of exercise training [60–62]. The effect of such training on survival or other postoperative outcomes within the older frail surgical population has not been evaluated.

Studies of exercise training in heart failure have shown improvement in symptoms and exercise capacity in addition to favourable changes in skeletal myopathy, endothelial function and cytokine expression [63]. Although not directly comparable with the frail population, the underlying cytokine mechanisms behind these syndromes may overlap, given the role of TNF in the 'cardiac cachexia' of chronic heart failure. The benefit and tolerability of exercise programmes tailored specifically for older frail patients with heart failure should pave the way for research into the potential therapeutic role of exercise training within the frail surgical population [64, 65]. A Cochrane review has found a positive link between progressive resistance training and strength and function, but the role of power versus strength training and the longitudinal view of exercise in modifying sarcopenia and frailty is still unclear [66].

### Using nutrition to modify frailty

Although the anaemia associated with frailty is likely to be related, at least in part, to inflammatory changes associated with the syndrome, within the older population anaemia can also be considered a surrogate marker of nutrition. The role of treating anaemia preoperatively in elective orthopaedic patients is now accepted as a method of reducing morbidity and mortality in this older surgical group [67]. Current recommendations suggest replacing iron, vitamin B12 and folate at least 28 days before scheduled elective surgery [67]. The impact of improving other nutritional deficiencies on the severity of frailty is less well understood. Despite the association observed between 25-hydroxyvitamin D and frailty [56], nutritional supplementation (multi-nutrient supplementation and vitamin D) in combination with physical activity intervention does not seem to independently improve the function of frail older people [61, 68]. Considering the overlapping geriatric syndrome of sarcopenia, evidence from a recent systematic review suggests that vitamin D supplementation may be





**Figure 1.** Overlapping geriatric syndromes.

indicated to combat sarcopenia in those with low vitamin D levels [69]. The role of nutritional intake may play a part in the development of sarcopenia and evidence supports the potential role of increased protein intake as a therapeutic intervention in targeting sarcopenia. Controversy exists regarding the amount of protein supplementation and the manner in which this should be taken [70, 71]. With a move towards promoting nutrition as part of enhanced recovery programmes in colorectal surgery [72–74], the potential effect that nutritional supplementation may have on surgical outcomes in frail individuals should be explored.

### Using drug therapies to modify frailty

At present there is no consensus regarding the potential pharmacological modification of frailty or related geriatric syndromes [75]. Potential modulators of frailty include anabolic steroids, growth hormone and anticytokine agents [53]. Other strategies have been employed in sarcopenic patients with varying degrees of benefit. Testosterone and growth hormone are not currently recommended in sarcopenia due to lack of efficacy and unacceptable side-effect profiles and more work is needed on antioxidants and creatine [70]. However, a randomised controlled trial has shown that improved exercise capacity and fewer falls were seen in older patients with impairment in ADL, given angiotensin-converting enzyme (ACE) inhibitors, and this has attracted interest in the potential role of ACE inhibitors in preventing or reducing the progression of sarcopenia

[76]. The mechanisms by which ACE inhibitors may have an effect on sarcopenia or body composition are not understood [70].

### The impact of other factors on modifying frailty

A positive affect has been shown to significantly lower the risk of becoming frail [77]. Depression is an independent correlate of frailty in community-dwelling older people [78]. The role of treating depression, on reducing the implications of frailty within the older surgical population, remains less clear. Frailty has been shown to be independently associated with individual and neighbourhood socioeconomic factors [79]. This implies that policies targeting frailty in older adults may need to incorporate the wider social context of frailty.

### Unanswered questions and future research

In summary, frailty is predictive of mortality, postoperative complications and institutional discharge in older patients undergoing cardiac and non-cardiac surgery. The evidence suggests that aspects of frailty may be amenable to intervention that could potentially reduce adverse outcomes. In the surgical population this raises numerous questions that are currently unanswered by the literature:

- Should we routinely measure frailty in the preoperative older patient?

- Which tool, biomarker or functional assessment would be most clinically applicable?
- Who should be measuring this?
- Is the measurement of frailty most useful in predicting surgical risk or in identifying issues for modification and optimisation?
- What should our 'frailty intervention' be?
- When should the intervention be employed with respect to the timing of surgery?
- What about emergency surgery?
- How about cancer surgery?
- Do interventions positively impact adverse postoperative outcomes?

Research into frailty is needed to answer these questions. Future work should be directed at refining diagnostic and screening tools, better understanding the epidemiology and natural history of frailty and understanding the potential for intervention both in terms of inflammatory modulation [53] and clinical intervention [25, 37, 80, 81]. This potential for proactive intervention and modification of the features of frailty may positively impact surgical outcomes in older patients in the future [82–86].

### Key points

- An increasing number of frail older patients are undergoing surgical procedures.
- Frailty is an independent risk factor for adverse postoperative outcomes.
- The evidence that aspects of frailty can be modified is emerging.
- Optimisation of frail older patients prior to surgical procedures could improve postoperative outcomes.

### Supplementary data

Supplementary data mentioned in the text is available to subscribers in *Age and Ageing* online.

### References

- PLEASE NOTE: The long list of references supporting this review has meant that only the most important are listed here and are represented by bold type throughout the text. The full list of references is available as Supplementary data are available in *Age and Ageing* online, Appendix 1
- Hamel MB, Henderson WG, Khuri SF, Daley J. Surgical outcomes for patients aged 80 and older: morbidity and mortality from major noncardiac surgery. *J Am Geriatr Soc* 2005; 53: 424–9.
  - Polanczyk CA, Marcantonio E, Goldman L *et al.* Impact of age on perioperative complications and length of stay in patients undergoing noncardiac surgery. *Ann Intern Med* 2001; 134: 637–43.
  - Dasgupta M, Rolfson DB, Stolee P, Borrie MJ, Speechley M. Frailty is associated with postoperative complications in older adults with medical problems. *Arch Gerontol Geriatr* 2009; 48: 78–83.
  - Makary MA, Segev DL, Pronovost PJ *et al.* Frailty as a predictor of surgical outcomes in older patients. *J Am Coll Surg* 2010; 210: 901–8.
  - 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.
  - Afilalo J, Eisenberg MJ, Morin JF *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.
  - Lee DH, Buth KJ, Martin BJ, Yip AM, Hirsch GM. Frail patients are at increased risk for mortality and prolonged institutional care after cardiac surgery. *Circulation* 2010; 121: 973–8.
  - Rockwood K. What would make a definition of frailty successful? *Age Ageing* 2005; 34: 432–4.
  - 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.
  - Martin FC, Brighton P. Frailty: different tools for different purposes? *Age Ageing* 2008; 37: 129–31.
  - 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: M146–56.
  - Rockwood K, Mitnitski A, Song X, Steen B, Skoog I. Long-term risks of death and institutionalization of elderly people in relation to deficit accumulation at age 70. *J Am Geriatr Soc* 2006; 54: 975–9.
  - Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. *Age Ageing* 2006; 35: 526–9.
  - Klidjian AM, Foster KJ, Kammerling RM, Cooper A, Karran SJ. Relation of anthropometric and dynamometric variables to serious postoperative complications. *Br Med J* 1980; 281: 899–901.
  - Hilmer SN, Perera V, Mitchell S *et al.* The assessment of frailty in older people in acute care. *Australas J Ageing* 2009; 28: 182–8.
  - Robinson TN, Eiseman B, Wallace JI *et al.* Redefining geriatric preoperative assessment using frailty, disability and comorbidity. *Ann Surg* 2009; 250: 449–55.
  - Robinson TN, Wallace JI, Wu DS *et al.* Accumulated frailty characteristics predict postoperative discharge institutionalization in the geriatric patient. *J Am Coll Surg* 2011; 213: 37–42.
  - Pol RA, van Leeuwen BL, Visser L *et al.* Standardised frailty indicator as predictor for postoperative delirium after vascular surgery: a prospective cohort study. *Eur J Vasc Endovasc Surg* 2011; 42: 824–30.

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