ICU

MANAGEMENT & PRACTICE

INTENSIVE CARE - EMERGENCY MEDICINE - ANAESTHESIOLOGY

VOLUME 20 - ISSUE 1 -2020

COVID -19 Challenges

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Ultrasound in Times of COVID-19

The potential clinical utility of ultrasound modalities in the COVID-19 patient, the limitations, evidence base and governance over point of care ultrasound images during a pandemic and a discussion on whether the hype surrounding Lung Ultrasound (LUS) is justified.

Introduction

The use of ultrasound outside radiology has already become well established within many of the acute specialties, such as critical care and emergency medicine. Critical care ultrasound (CCUS) takes place at the point of care. It has many advantages:

- Non-invasive
- Negates the need to expose the patient to ionising radiation
- Associated with minimal logistical disruption, being performed at the bedside
- Repeatable (Huang et al. 2020)
- Quick to perform
- Low cost

Many of these qualities have become particularly relevant in the current climate of the COVID-19 pandemic we are facing, where moving patients with COVID-19 around the hospital, in order to perform imaging studies, comes with significant risks. Sending patients elsewhere in order to perform other imaging studies removes them from a place of isolation/infection quarantine, to non-infected areas. This places other staff, patients and the general public at significant risk of contamination.

There has been much fixation with COVID-19 being a disease solely affecting the lungs. In this article, we will discuss the potential clinical utility of the other ultrasound modalities in the COVID-19 patient. We will also discuss the limitations, evidence base and governance over point of care ultrasound images during a pandemic. Indeed, is all of the hype surrounding Lung Ultrasound (LUS), justified, as it has certainly received the limelight?

What is the Advantage of Ultrasound in Times of Pandemic?

During the Ebola outbreak, Henwood describes ultrasound as being fairly pivotal to patient care and assessment (Henwood 2019). It assisted them in the support of the pregnant patient, as well as in the assessment of respiratory status. Moreover, it aided them in volume assessment, which is always a contentious issue in febrile states. They state that it narrowed down their differential diagnosis list and also allowed them to piece together the clinical puzzle in resource-limited settings where they lacked other diagnostic imaging tools-essentially utilising whole body ultrasound as their 5th pillar of clinical examination (Narula et al. 2018).

Interestingly, and a point we make on many occasions, they state that it helped them to conserve valuable PPE, as they could utilise even relatively unskilled sonographers to perform the examinations. They placed an expert user outside of the clinical area on standby to interpret the images; the first form of telemedicine if you will. Handheld ultrasound devices were used (presumably due to affordability within resource constrained areas), and linked to Wi-Fi in order to send images to providers in low-risk zones. The chosen devices could be cleaned easily between patients, so minimising the spread of infection.

Adapted from Peng et al.	Adapted from Volpicelli et al.
Thickening of the pleural line with pleural line irregularity. B-lines in a variety of patterns including focal, multifocal, and confluent. Consolidations in a variety of patterns including multifocal small, non-translobar, and translobar with occasional mobile air bronchograms. Appearance of A lines during recovery phase. Large pleural effusions are uncommon.	**Intermediate probability of COVID-19** Small, very irregular consolidations at the two bases without effusion or with very limited anechoic effusion. Focal unilateral interstitial syndrome (multiple separated B-lines) with or without irregular pleural line. Bilateral focal areas of interstitial syndrome with well-separated B-lines with or without small consolidations. **High probability of COVID-19** Bilateral, patchy distribution of multiple cluster areas with the light beam sign, alternating with areas with multiple separated and coalescent B-lines and well-demarcated separation from large "spared" areas. The pleural line can be regular, irregular or fragmented. Sliding is usually preserved in all but severe cases. Multiple small consolidations limited to the periphery of the lungs A light beam may be visualised below small peripheral consolidations and zones with irregular pleural line.

Table 1: Summary of sonographic characteristics of LUS in COVID-19 infection

How Does LUS Compare to Plain Chest Radiography (CXR) and Computed Tomography (CT)?

Chest imaging is important for diagnostic and prognostic reasons. The ideal test would be quick, reliable, reproducible, deliverable at the bedside and have a high sensitivity and specificity. Currently, the main modalities used are CXR, CT and in some centres, LUS. Small studies have looked at the sensitivity and specificity of CT compared to RT-PCR, and CT currently has the highest sensitivity of any test for COVID-19 (Fang et al. 2020).

Almost all patients will receive a chest radiograph, but plain chest radiography has a poor sensitivity as compared with CT and LUS. Plain radiographs may miss up to 40% of confirmed COVID-19 cases. One reason why plain radiography has a reported low sensitivity is that virus particles are small and lodge in terminal alveoli close to the pleural interface. These areas are well visualised on CT and LUS, but are more difficult to see on plain imaging (Huang et al. 2020; Tian et al. 2020).

Thoracic CT imaging has been proposed as a primary screening tool for COVID-19 detection, since it performs better than PCR. Lung abnormalities on CT may precede physical symptoms of COVID-19, thus allowing early detection, isolation and management of infected patients.

However CT is a finite resource and may not be available in some healthcare settings. Decontamination protocols are not well defined and are time consuming. The practicalities of moving critically ill patients to CT are difficult and thus a risk benefit approach has been taken by some clinicians, reserving this technology for patients with complications of COVID-19 infection or when other causes of illness such as pulmonary embolism are suspected.

LUS has been recommended by Italian emergency physicians as an ideal form of imaging for evaluation of suspected COVID-19 infection. The authors discuss portable and inexpensive handheld US devices, ease of use by the treating clinician at the bedside and reduced movement of patients to the radiology department and reduced exposure of other healthcare workers (HCW).

Clinical Utility

The radiological appearance of patients with COVID-19, using traditional chest imaging techniques such as CXR and CT, have been described in the literature (Inciardi et al. 2020). Indeed, radiological changes are thought to precede the onset of the symptoms themselves. Compared to these modalities, lung ultrasound (LUS) has many advantages. It reduces the dependence on CT and improves risk stratification, while maintaining isolation protocols. This minimises contamination of staff

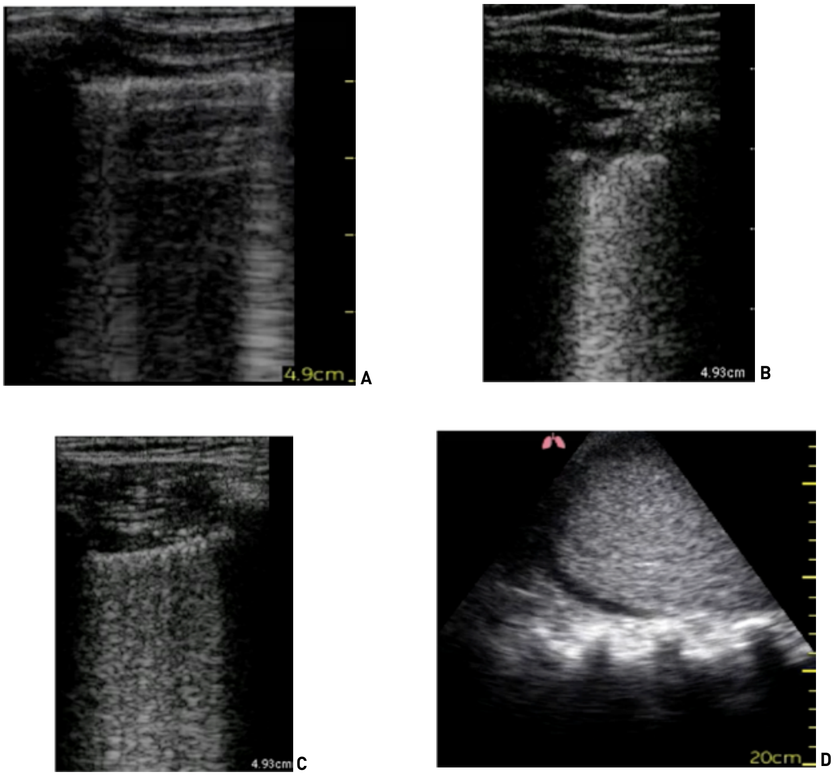

Figure 1: a) Linear view LUS, with skip B-line profiling and preserved A-line profiling in early COVID-19 pneumonitis; b) Confluent B-line profiling, sub-pleural consolidation and irregular thickened pleura in medium severity COVID-19 pneumonitis; c) Confluent B-line profiling and obliteration of all A-lines in severe COVID-19 pneumonitis; d) Basal consolidation, parapneumonic effusion and spine sign seen at the base of a COVID-19 patient with severe pneumonitis.

and equipment.

Broadly speaking, ultrasound has 3 main uses:

1. The initial diagnosis of COVID-19
2. Assessment of disease severity along with history and other clinical examination
3. The ongoing management of the disease

LUS in COVID-19

LUS is the primary imaging modality for COVID-19 as respiratory symptoms are the herald of the disease (shortness of breath and exertional dyspnoea). However, gastrointestinal and neurological symptoms have also been reported in the literature. Early experience with LUS amongst colleagues in China found the following characteristics (Peng et al. 2020a; Volpicelli et al. 2020). The LUS features of patients with COVID19 are summarised in **Table 1**.

Overall, the characteristic changes in COVID-19 infection are similar to other viral pneumonitis (Yousef and De Luca 2018). Examples of the findings are shown in **Figure 1**.

The sonographic appearance depends upon the time course of the illness and the presence of other pre-existing or superimposed conditions. Clinical deterioration can be investigated using the other ultrasound modalities. These may include acute cardiomyopathy, acute pulmonary embolism, evidence of secondary or superadded infection, pleural effusions and pneumothorax. **Figure 2** shows the Focussed Ultrasound for Intensive Care pathway (FUSIC) pathway.

Two broad divisions or phenotypes have been proposed by Gattinoni et al. (2020); the "L"- and "H-" type.

H-Type

This phenotype is characterised by high lung elastance, low lung compliance and a significant accumulation of lung water. Similar to more traditional forms of ARDS, these patients are more difficult to ventilate and the use of PEEP may be beneficial during significant refractory hypoxic periods.

L-Type

Characterised by low lung elastance and higher compliance, such patients are 'easier' to ventilate. Hence, high PEEP levels may be detrimental during hypoxic episodes, with patients potentially benefiting from early proning.

Whilst it is tempting to discuss the phenotypes as two separate entities, it is likely that they represent ends of a continuous spectrum.

Lung ultrasound to direct ventilatory strategies

POCUS may differentiate the two lung patterns mentioned above:

1. Bilateral, diffuse, anterior, multiple B-lines with pleural abnormalities (H-type).
2. Normal anterior lung (or anterior lobar consolidation) with postero lateral basal atelectasis consolidation (L-type).

As the lung goes from aerated to non aerated, lung ultrasound appearances progress from A lines → a few B-lines → lots of B-lines → coalesced B-lines→ consolidation. Performing a PEEP or prone trial while monitoring lung appearances in real time could potentially give a guide to lung "recruitability," similar to studies performed in the early 2000s (Volpicelli et al. 2020), however there is no COVID-19 specific data on this technique.

Lung ultrasound to monitor extravascular lung water

PICCO studies have demonstrated that these patients have an increased amount of extravascular lung water (EVLW; Personal communications, April 2020). B-line density has been shown to correspond with increased extravascular lung water

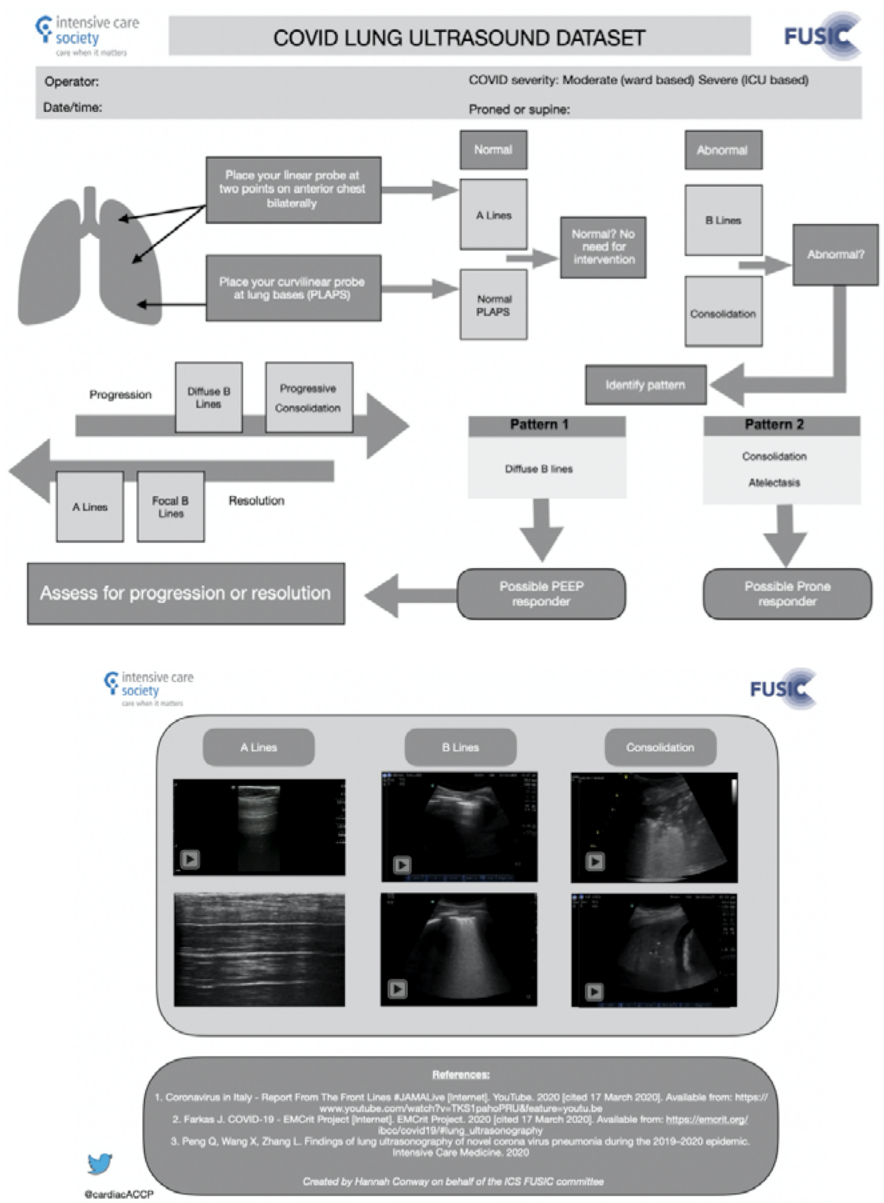

Figure 2: Focussed Ultrasound for Intensive Care pathway (FUSIC) pathway

in ARDS. LUS thus provides an attractive non-invasive monitor of such changes and can be used to assess the need for, and response to, diuretic therapy.

In patients with cardiovascular instability, fluid administration can be monitored by assessing the lungs for the appearance of increase in B-lines following a fluid bolus (Lichtenstein 2013). This is challenging in COVID-19 patients, as most will have B-lines already. Combining LUS with echocardiographic measures of stroke volume and fluid responsiveness can potentially increase the diagnostic accuracy and safety threshold of fluid therapy, but data on this approach is sparse.

Cardiac Ultrasound in COVID-19

Although predominantly affecting the lungs, COVID-19 can affect the cardiovascular system through several mechanisms. There are indirect effects on myocardial function, secondary to heart-lung interactions; this can be observed when high PEEP adversely affects the right ventricular afterload (Peng et al. 2020b).

There are also direct cardiotoxic viral effects; the virus has been isolated from myocardial tissue in case reports (Tavazzi et al. 2020). This has anecdotally manifested as an acute deterioration 7 to 10 days into the course of the illness. The sequence of events seems to be in keeping with a generalised hyper-inflammatory process, with corresponding rise in laboratory biomarkers such as CRP, ferritin, D-dimers etc. This inflammatory response can cause myocardial injury with focal or global myocardial inflammation, necrosis and ventricular dysfunction. A recent case series from Wuhan suggested a 19.7% incidence of myocardial injury in a cohort of hospitalised patients with COVID-19 (Bonow et al. 2020).

CCUS is perfectly suited to monitor these effects at the bedside. Heart-lung interactions can be monitored using LV and RV size and function, in time with the respiratory cycle, as previously described. Fluid status, ventilation, and PEEP can then be tailored to optimise cardiac function.

The downstream effects of severe LV or RV dysfunction on systemic organ perfusion can also be monitored using CCUS. Profound RV dysfunction can manifest as hepatic and renal dysfunction, visible on CCUS as abnormalities in hepatic, portal and renal blood flow (Beaubien-Souligny et al. 2020). Management of a congestive phenotype of organ failure would include fluid removal, inotropic support, pulmonary vasodilators, and venovenous ECMO.

Vascular Ultrasound in COVID-19

Vascular access

COVID-19 patients who are critically unwell will require central venous access either for drug administration, renal replacement therapy or ECMO. Ultrasound guidance has been proven to increase first pass success rate while reducing complications during vascular access.

Ultrasound guidance also facilitates

access in the prone position, where the usual anatomy becomes distorted (Chen et al. 2017). Post placement, line position can be confirmed using an ultrasound only technique, minimising the use of CXR (Saul et al. 2015).

Thromboembolic disease

Patients with severe COVID-19 are immobile and have a hyper-inflammatory state. These, in combination, lead to a hypercoagulable state. There is also the possibility of endothelial cell activation/damage due to binding of the virus to the ACE2 receptor. Hence, it seems obvious that they are at increased risk of developing deep venous thrombosis and subsequently pulmonary embolus. Optimal thromboprophylaxis in COVID-19 patients is unknown. The use of ultrasound by the bedside clinician to assess for DVT is quick, easy and sensitive; there may be a role for monitoring these patients for the development of VTE and changing anticoagulation strategy as felt appropriate (Hunt et al. 2020).

Airway Ultrasound in COVID-19

Patients with COVID-19 can present in severe hypoxic respiratory failure where intubation is performed as an emergency procedure. Previous data has shown that intubation outside the theatre environment confers a higher risk of morbidity and mortality with an increased incidence of difficult airway scenarios (Cook et al. 2011).

Upper airway ultrasound is a convenient, cost-effective and reproducible tool. The integration of upper airway ultrasound to complement pre-intubation airway screening may be the way forward, and a future standard of care.

The use of ultrasound has 3 main advantages:

1. The assessment of upper airway anatomy
2. Confirmation of appropriate airway device placement
3. Aiding in placement of tracheostomy

It is beyond the scope of this article to describe the sonoanatomy of the upper airway.

Assessment

Ultrasound may permit appropriate risk assessment and hence airway management strategy formulation. Various scoring systems have been described to formulate a more consistent and robust approach to this strategy.

On a related matter, in the 'cannot intubate, cannot ventilate' scenario, timely identification of the cricothyroid membrane to facilitate emergency front of neck access is lifesaving. This is even more advantageous if the identification is done under controlled circumstances preemptively (You-Ten et al. 2018).

Airway device placement

Ultrasound can be used to confirm appropriate placement of the endotracheal tube. This is especially important in resource limited environments, where the availability of capnography is not universal.

Tracheostomy

Further down the patient clinical time course, it is expected that a proportion of patients recovering from COVID-19 will require tracheostomies. Traditionally, the use of bronchoscopy to guide percutaneous tracheostomies have been advocated. However this is recognised as a high-risk, aerosol generating procedure which exposes the operator to significant risk. The use of ultrasound to replace bronchoscopy-guided PCT has been described and should be considered if appropriate expertise be available (Ravi and Vijay 2015).

Abdominal Ultrasound

Hepatic complications of critical illness include portal vein thrombosis, cholecystitis, biliary stasis, and hepatic congestion as a result of right heart failure. These can be readily detected by CCUS.

Data from the UK has shown that 20% of patients have required renal replacement therapy (20- ICNARC data). Ultrasonography is useful for ruling out obstructive uropathy in these patients. More advanced applications involve using doppler imaging techniques for detecting alterations in renal arterial and venous flow; there is currently very limited COVID-19 specific data on this modality.

Haemophagocytic lymphohistiocytosis (HLH) is a recognised complication of COVID-19, and manifests as multiple cytopaenias, a high ferritin, and hepatosplenomegaly. CCUS can be used to monitor and detect organomegaly if it were to occur (Tveiten et al. 2020).

Intra-abdominal free fluid, ileus, NG tube position, and free intraabdominal air can be detected with CCUS. It would seem prudent to utilise CCUS expertise, where available, as the first line imaging modality in these patients, reserving CT for where there is diagnostic ambiguity or inadequate imaging. This has been the practice of the Chinese Critical Ultrasound Group (Personal communications, March 2020)

Learning and Research During COVID-19

During the COVID-19 pandemic, there are two compelling (and competing) priorities: treating patients and learning new knowledge including skills and treatment.

Exploiting existing knowledge or beliefs is helpful in the short-term, but not in the long-term. Conversely, learning something new is risky in the short-term, but essential in the long-term. In this uncertain situation, we need to try and do both simultaneously.

Like any other skill, there is a learning curve associated with CCUS and the various accreditation programmes available require a period of mentorship as well as assessment (Smith et al. 2020). Many regulatory bodies are pausing formal training programmes in ultrasound during this period; however, abbreviated focused training pathways for very specific subsets of CCUS have become available, most noticeably with lung ultrasound.

The decisions on how to deploy CCUS should be taken on an institutional or indeed national level. An example is the UK's Intensive Care Society National COVID-19 Point-of-Care Ultrasound Evaluation exercise (FUSIC 2020).

Governance

CCUS is a diagnostic modality and as such should be subject to quality assurance, similar to any other diagnostic modality in the hospital (laboratory tests and other forms of radiology). A system should be in place to assess the quality of both individual sonographers and the interpretation of these images.

The authors suggest that any images used for clinical decision making are stored, ideally on a patient archiving system. A minimum dataset should be suggested and maintained. Individual sonographer case review should be regularly undertaken to ensure standards are kept- this could be in the form of a monthly audit or case presentation. Units should align themselves with national policy for each diagnostic modality used wherever possible, such as recent guidelines on the use of POCUS written by EFSUMB, the Intensive Care Society, and BMUS.

The individuals who will perform governance will likely vary from institution to institution - the authors would suggest a mix of radiologists, cardiologists, and acute physicians would cover all bases of CCUS.

Cleaning & Disinfection Protocols

Decontamination strategies are vital to prevent patient-to-patient COVID-19 transmission as well as patient to healthcare worker COVID-19 transmission.

Several international bodies have described US machine specific COVID-19 cleaning and disinfection protocols (BMUS 2020; CPoCUS 2020).

The following (**Table 2**) are best practice summary points drawn from international standards and should be considered when using US with suspected COVID-19 patients (ACEP.org).

Place a dedicated US machine in the COVID-19 examination area of your Intensive Care Unit
Use disposable single-use gel packets rather than gel bottle
Wear standard personal protective equipment when performing LUS and wear gloves when moving the machine from cubicle to cubicle
Strip away all leads, gel bottles extra buckets, straps from your machine
Clean cables, screen, legs, wheels
Cover the transducer with plastic sheath
Use a touchscreen device to minimise keyboard, knob handle handling
Wait for up to 3 minutes 'dry time' after using disinfectant wipes before you use the machine again
Use your machine in battery mode - precharge at all times, remove all cables
Use a handheld device eg. Lumify or Butterfly systems with the advantage that images are uploaded to the cloud for remote reviewing

Table 2: Best practice summary points

This material has been 'crowdsourced' or extrapolated from shared knowledge of global expert user groups. There are many practical and innovative approaches to US machine decontamination available on social media, collated under the hashtag #POCUSforCOVID (ultrasoundtraining.com.au/news/covid-19-pocus-resources).

Conclusion

COVID-19 is a novel disease and hence our understanding of the entire disease pathology, management and imaging features are still evolving. There is much that remains unknown and hence the evidence base for the use of ultrasound in the pandemic is weak. When considering the use of any intervention or investigations, the practicalities and logistics need to be taken into consideration.

Conflict of Interest

Adrian Wong has received speaking honorarium from the industry. Olusegun Olusanya has received honoraria to teach ultrasound. Jonathan Wilkinson has received honoraria from GE Healthcare. Other authors declare no conflict of interest. ■

Key Points

- LUS has been extensively discussed in the literature.
  - It is a well established tool in the diagnosis of acute respiratory failure.
  - It demonstrates clear patterns in COVID-19 infection, many of which are very similar to other patterns of viral pneumonitis.
  - CXR is a poor screening test for COVID-19 compared with CT. CT may be better used for screening for the complications arising from COVID-19 infection.
- Cardiac, abdominal and vascular ultrasound complement LUS and allows for a holistic, whole body approach in the assessment of patients with COVID-19.
- With the conveniences ultrasound affords, it is a highly useful decision support tool in COVID-19.

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