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Abstract:	As clinicians working in critical care, it is our duty to provide all of our patients with the high-quality care they deserve, regardless of their gender identity. The transgender community continues to suffer discrimination from the media, politicians and general public. As healthcare workers we often pride ourselves on our ability to safely care for all patients. However, there remains a distinct lack of understanding surrounding the care of critically ill transgender patients. This is likely in part because the specific care of transgender patients is not included in the Faculty of Intensive Care Medicine's, Royal College of Anaesthetists', Royal College of Physician's, or Royal College of Emergency Medicine's curriculum. There are several important considerations relevant for transgender patients in critical care including anatomical changes to the airway, alterations to respiratory and cardiovascular physiology, and management of hormone therapy. Alongside this, there are simple but important social factors that exist, such as the use of patient pronouns and ensuring admittance to correctly gendered wards. In this review we will address the key points relevant to the care of transgender patients in critical care and provide suggestions on how education on the subject may be improved.

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Abstract

As clinicians working in critical care, it is our duty to provide all of our patients with the high-quality care they deserve, regardless of their gender identity. The transgender community continues to suffer discrimination from the media, politicians and general public. As healthcare workers we often pride ourselves on our ability to safely care for all patients. However, there remains a distinct lack of understanding surrounding the care of critically ill transgender patients. This is likely in part because the specific care of transgender patients is not included in the Faculty of Intensive Care Medicine's, Royal College of Anaesthetists', Royal College of Physician's, or Royal College of Emergency Medicine's curriculum. There are several important considerations relevant for transgender patients in critical care including anatomical changes to the airway, alterations to respiratory and cardiovascular physiology, and management of hormone therapy. Alongside this, there are simple but important social factors that exist, such as the use of patient pronouns and ensuring admittance to correctly gendered wards. In this review we will address the key points relevant to the care of transgender patients in critical care and provide suggestions on how education on the subject may be improved.

Introduction

As critical care clinicians it is our duty to provide the best care we can to all patients, regardless of their gender identity. To do this, it is vital we are cognisant of the specific anatomical, physiological and psychological considerations present when caring for transgender patients.

There are currently estimated to be between 200,000 – 600,000 people in the UK that openly identify as transgender.(1,2) Transgender patients face considerable healthcare disparities, with 70% diagnosed with depression and >40% having attempted suicide.(3,4) Being trans is not a mental illness in itself, but mental health distress results largely from widespread discrimination or experiences of verbal or physical abuse in many aspects of life.(5) This includes misgendering, misunderstanding, and even refusal of care by healthcare providers. Many transgender people avoid healthcare interactions due to fear of discrimination, which can lead to delayed diagnosis and delayed presentations to emergency services.(3,4) A clinician's interaction with a transgender person can therefore have significant impact upon distress and mental health.

Medical education specific to the transgender patient remains poor, which in turn contributes to these poor healthcare experiences. Forty-one percent of transgender patients state they feel their healthcare needs are not understood by their clinicians.(1) Our recent survey of UK anaesthetists found a lack of confidence regarding the perioperative care of transgender patients, with the median confidence score on a Likert scale of 0 to 10 for assessment of airway, respiratory or cardiovascular concerns being 4, 3, and 3 respectively. Eighty-six percent of respondents stated they felt postgraduate bodies should deliver education on transgender healthcare.(6) To date, these needs are not addressed in the Faculty of Intensive Care Medicine (FICM), Royal College of Anaesthetists (RCoA), Royal College of Emergency Medicine (RCEM) or Royal College of Physicians (RCP) curricula throughout any stage of training.(7–10) Improving our means of recognising, understanding, and addressing the needs of transgender patients is a central factor in our ability to provide optimal care.

There are several important considerations to be aware of when caring for transgender patients in critical care (Figure 1). These include changes to the airway, alterations to cardiovascular risk factors, and management of hormone therapy, with many of these becoming particularly pertinent in the event of a time-pressured emergency.(11,12) Holistic, person-centred care of transgender patients also includes specific sensitivity around communication and use of language; consent and confidentiality; and organisational factors. Focused education and training will aid the clinician to care for a transgender patient safely and effectively. In this review we will highlight the important points relevant to the critically ill transgender patient and discuss how education on the subject could be improved.

Terminology

It is important to understand some of the basic terminology used when discussing gender. Terminology within the transgender community is continually evolving and is very personal to the individual. We have chosen the terminology used in this article for familiarity and consistency after consultation with experts working within transgender healthcare but acknowledge that this may not be the language some individuals identify with.

The World Health Organisation (WHO) defines sex as the different biological and physical characteristics of males and female, such as reproductive organs.(13) This is most often assigned at birth as either male or female. In contrast, gender refers to socially constructed characteristics of men and women, such as gender norms and roles, and varies between societies. Gender identity refers to an individual's internal identity across a gender spectrum. This may differ from the sex they were assigned at birth, or the gender roles society expects of them. Gender-expression is how an individual communicates their gender identity.(11,13)

The term cisgender refers to an individual whose gender identity is the same as the sex they were assigned at birth. In contrast, a transgender individual is one whose gender identity differs from the sex they were assigned at birth and includes people with binary (male or female) and non-binary identities.

Transgender people may choose to affirm their gender in different ways. Up to 29% may opt solely for social gender affirmation – which may include change to their gender pronouns, name and external appearance such as clothing and hair, without medical intervention.(3)

As a separate group, 52% of transgender individuals have undergone or are currently undergoing medical intervention. A further 25% have not yet undergone any medical intervention but wish to in the future.(1) This range of treatments, commonly known as gender-affirming therapy, includes a range of pharmacological therapies (usually involving hormonal medication) and surgical interventions (including a range of airway, maxillofacial, chest, urological, and gynaecological procedures). Colloquially, 'top surgery' is any surgical procedure that changes the appearance of a transgender patient's chest, while 'bottom surgery' is a term used for gender affirming surgery involving the genitals.

Anatomical changes

Trans men and women

patients may undergo an array of gender-affirming surgical procedures of relevance to critical care clinicians.

Airway

It is well-known that the incidence of difficult intubation for any patient in a critical care setting is higher than for other patient cohorts. This, coupled with the reduction is safe apnoeic time before desaturation (14) makes it vital that key factors contributing to potential airway difficult are identified

early and a clear plan discussed. There may be additional challenges posed to airway management in transgender patients that have undergone specific gender-affirming treatments.

Maxillofacial procedures

Transgender females may undergo cosmetic feminisation procedures, to align their physical appearance with their gender identity. These procedures can make the standard airway assessment misleading, and may include:

- mandible reduction – may result in crowding of the oropharynx
- chin augmentation – reducing the reliability of the perceived thyro-mental distance
- rhinoplasty – may affect instrumentation of the nose.(12,15)

Vocal cord surgery

Alterations to vocal cord length and tension may be performed to change a patient's vocal pitch. These procedures may have significant effects on airway techniques used. Examples of surgical options include:

Vocal Feminisation surgery

- Endoscopic glottoplasty– The anterior portion of the vocal cords are sutured resulting in a reduction in the glottic aperture of approximately 33% (similar to that of a cis-female). Endotracheal tube (ETT) size should be chosen with this in mind. A smaller tube may be required (Figure 2).
- Cricothyroid approximation– Vocal cord tension is increased by anterior-inferior movement of the thyroid cartilage and posterior-superior movement of the cricoid cartilage. An important repercussion of this is potential loss of the cricothyroid membrane, making front of neck access impossible in a 'cannot intubate, cannot oxygenate' scenario. Thus, an alternative 'plan D' must be discussed in advance.

Vocal masculinisation surgery

- Thyroplasty type III– the aim of this procedure is to reduce vocal cord tension. A vertically long rectangular piece is removed from each thyroid ala with the anterior commissure of the glottis moving dorsally and thus relaxing the vocal cords.(12,15)

It is important to note that patients may achieve considerable changes in vocal character through voice training techniques and speech and language therapy, and so it is important to ask the patient directly about any vocal cord surgeries if possible.

Cosmetic feminisation procedures that affect the airway may have also been performed. One example is chondroplasty, also referred to as tracheal shave. In this procedure, the size of the thyroid cartilage is shaved down to reduce its size to give the throat a smoother and less angular appearance. Potential complications include removal of excess tissue resulting in narrowing of the trachea or damage to the vocal cords.

Airway instrumentation within the three months following vocal cord surgery should be avoided where possible. If elective airway management is required in this period, ideally a supraglottic device should be considered where appropriate, otherwise a micro-laryngeal tube should be considered to avoid airway trauma. In the emergency setting, a definitive airway is likely to be required and the above may not be possible. The priority must be securing a safe airway with adequate oxygenation and ventilation.(12,15) In such scenarios, preparation should be made in anticipation of a potentially difficult airway in line with the Difficult Airway Society guidelines, with ETT size selected accordingly.(16) History taking is vital to ascertain if cricothyroid approximation surgery has indeed taken place, and whether emergency front of neck access is likely to be difficult, or even impossible.

At present, these surgical procedures are relatively uncommon in the NHS and UK population, however taking the time to ascertain if the patient has had them will be vital in the event of an airway emergency. Of note, testosterone therapy alone can result in an increase in mass and thickening of

the vocal cords and thus a decrease in the size of the glottic aperture in people assigned female at birth.(17)

Respiratory

Transgender patients may undergo 'top surgery' either to remove or enhance breast tissue. Examples of masculinising procedures include mastectomy and masculinising breast augmentation.(18,19) Complications of mastectomy remain the same as for cis females and include haematoma, seroma and nipple complications. Examples of feminising procedures include breast augmentation, mammoplasty with insertion of implants or lipofilling. This may be of relevance if transgender patients require ventilation in the prone position.(11,18)

Another important practice to be aware of is chest binding (Figure 3). Trans male or non-binary patients who have not undergone top surgery may practice chest binding, whereby a bandage or specifically designed binder is wrapped very tightly around the patient's chest to flatten their breast tissue.(20) Whilst the implications of this practice on ventilation have not been directly investigated, chest wall strapping is a technique that has been used to investigate pulmonary mechanics previously.

Chest wall strapping results in a decrease in total lung capacity, functional residual capacity, residual volume and expiratory reserve volume.(21) One may reasonably consider that chest binding has a similar effect on respiratory mechanics and therefore binders should be removed prior to the initiation of mechanical ventilation and indeed when ventilatory failure is present. If possible, this should be clearly discussed with the patient, ensuring they understand the reason for binder removal and agree with the management plan. If the patient is unable to tell you if they have a binder on due to critical illness, this should be examined for and removed if thought to be impairing respiratory dynamics. When the patient does become alert enough again, the removal should be sensitively explained to them, and the binder replaced as soon as practical.

Urological

Transgender people may undergo a spectrum of different gender-affirming gynaecological and urological procedures or 'bottom surgery'.(22) For trans women these can include:

- Vaginoplasty
- Clitoroplasty
- Vulvoplasty
- Orchidectomy
- Penectomy

For trans men surgical options include:

- Hysterectomy
- Oophorectomy / total bilateral salpingo-oophorectomy
- Urethral reconstruction
- Metoidioplasty or phalloplasty
- Vaginectomy
- Scrotoplasty

There is a high risk of post-operative complications following urological surgery, including urinary tract infections, stricture and fistula formations. The risk of uretheral damage can be high, especially in unconscious or sedated patients and thus caution should be taken when catheterising a patient. Specialised urological input may be required.(11,18,22)

Pharmacological therapy

Medical gender-affirming therapy can involve a range of hormone treatments: these may be masculinising therapy or feminising therapy.(23–26)

Masculinising hormone therapy

Testosterone is the mainstay of masculinising hormone therapy. It may be administered intramuscularly (IM) or subcutaneously (SC) using short (2-4 weeks) or long acting (12 weeks) formulations, or daily via a transdermal preparation.(25) Examples of common hormone regimens include:

- Testosterone undecanoate (IM) – 1000mg every 12 weeks (Nebido)
- Testosterone enanthate (SC) – 50-200mg/week (Primoteston)
- Testosterone esters (IM) – 250mg monthly (Sustanon)
- Cypionate (IM) – 100-200mg every 10-14 days
- Testosterone gel 1% (top) – 2.5g-10g/day
- Testosterone patch (top) – 2.5-7.5mg/day

Only testosterone gels or injectables are prescribed in the UK. The injectables available are either short acting IM Sustanon or IM Enanthate every four weeks or long-acting IM Nebido every 12 weeks.

Physical effects

Effects of masculinising therapy may include lowered vocal pitch, increased body and facial hair, decreased fat mass, increased muscle mass, clitoral growth, increased haemoglobin to the male reference range, a potential decrease in breast tissue and a potential increase in bone density.(23,25)

Cardiovascular risks

The use of testosterone therapy may alter a patient's cardiovascular risk factors. Nota *et al*. found no associated increased in venous thromboembolism (VTE), myocardial infarction (MI), or stroke in trans men when compared to cis men. When compared to baseline incidence in cis women, taking testosterone therapy was associated with an increase in risk of MI (standardised incidence ratio of 3.69), but no increased risk of VTE or stroke (Table 1).(27)

Changes to laboratory results

Hormone therapy may alter baseline laboratory values.(28,29) Testosterone has been found to increase:

- Haemoglobin
- Haematocrit
- Creatinine
- Alanine aminotransferase
- Aspartate aminotransferase
- Triglycerides
- High-density lipoprotein

Feminising hormone therapy

This consists of the administration of oestradiol, often in conjunction with anti-androgens. Oestradiol may be administered orally, IM, or transdermal.(25) The goal is to raise oestradiol levels to within the female reference range, although exact values remain a point of ongoing discussion. Example oestradiol regimens include:

- Oral oestradiol valerate – 2-8mg/ day
- IM oestradiol – 5-20mg/ 2 weeks. This is not prescribed in the UK but is popular in the US, although we do not yet know the effects of long term high concentrations of oestrogen.
- Transdermal oestradiol – these include Estradiol patches 50-200mcg twice weekly and Estradiol gels (Sandrena) 0.5 – 4mg daily.

In addition to oestrogen, anti-androgens may be required in trans women who have not undergone orchidectomy, although normal female testosterone levels may be achieved with oestrodiol monotherapy alone.

Physical effects

Feminising hormone therapy has many of the opposite effects to testosterone. These include ~~a decrease in body and facial hair,~~ a decrease in muscle mass with an increase in fat mass, a potential decrease in bone mineral density, and an increase in breast tissue.(25,26) It is unlikely to influence vocal pitch and vocal/speech therapy is thus often required.

Cardiovascular risks

Feminising hormone therapy has been associated with an increased risk of MI when compared to cis women, but not when compared to cis men. Studies have also demonstrated an increase in risk of stroke when compared to both cis women and cis men. There is also demonstrated a five-fold and four-fold increase in VTE risk when compared to cis women and cis men respectively.(27)

Effects on laboratory results

Feminising hormone therapy has been found to have several effects on baseline laboratory results. These include a decrease in:

- Haemoglobin
- Haematocrit
- Creatinine
- Alanine aminotransferase
- Alkaline phosphatase
- Bilirubin
- Albumin
- Total calcium.(28,29)

Potential side effects of anti-androgens

There are several anti-androgens that can be chosen from. One of these is the potassium-sparing diuretic spironolactone. When used for gender affirming treatment it is administered at a 2-4 times higher dose than may be used for heart failure or liver disease. Regimens range from 100 – 400mg per

day. This is of relevance in the critically ill patient as, whilst not studied in this setting, such doses in the setting of renal impairment may lead to hyperkalaemia, hypovolaemia, and exacerbation an acute kidney injury.(18,23,25) Vigilant monitoring of potassium levels and renal function is therefore important in critical illness, and dose reduction may be required. If spironolactone needs to be stopped the dose does not need to be tapered.

Another anti-androgen licensed for use in the United Kingdom is the synthetic progesterone cyproterone acetate. It is generally well tolerated but potential side effects include fulminant liver failure at high doses, a dose-dependent increased risk of meningioma and exacerbation of depression.(18,25)

5alpha-reductase inhibitors such as finasteride and dutasteride may also be used in people with androgenic alopecia. The reported side effects include orthostatic hypotension.

Gonadotrophin-releasing hormone agonist analogues, such as leuprolide or triptorelin, may be used to suppress puberty in paediatric or adolescent transgender patients or to suppress menstruation in trans men. If used in trans women as an anti-androgen, they are normally prescribed alongside estradiol thus side effects rarely occur, but could include hot flushes, depression and a potential decrease in bone-mineral density if estradiol is ceased.(18,25)

Drug dosing

As with many other factors in their care, there is a paucity of data regarding appropriate drug dosing of all medications for patients at any point in their gender-affirmation process. It remains unclear how gender-affirming hormone therapy affects renal clearance and the ideal body weight (IBW) of transgender patients. Once established on hormone therapy, lean body mass and serum creatinine are consistent with that of their affirmed gender (and not the sex which they were assigned at birth). A transgender patient's body composition will start to show signs of change to their affirmed gender

after around three months of hormone therapy. After six months of hormone therapy, it is acceptable to calculate a patient's creatinine clearance and IBW based on the patient's affirmed gender. (27)

This general guidance will also apply to use of total intravenous anaesthesia (TIVA). All pharmocokinetic models require a programmed gender for the patient, and we know that lean body mass will start to resemble that of the affirmed gender at around three months of hormone therapy. There is no guidance available to date, but it is generally thought that after three months or hormone therapy, use of the patient's affirmed gender for the TIVA model will be appropriate. Given the potential for unpredictable effect site concentrations, clinicians should use additional monitoring including processed electroencephalogram as standard.(8)

General considerations

Holistic and psychological considerations are equally as important as the considerations already discussed. This remains poorly taught and understood by clinicians, yet one that can easily transform a patient's experience.

A simple place to start is by ensuring use of the correct name and pronouns. This can be easily achieved by asking a patient their pronouns, for instance he/him/his for patients that identify as male, she/her/hers for patients that identify as female and they/them/theirs for patients that identify as non-binary. Once the patient's preferred name and pronouns have been established it is important this information is handed over to relevant staff members to ensure smooth continuity of care.

It is also important that patients are admitted to the correctly gendered ward; this means either to a ward or section of the intensive care unit that aligns with their gender identity, a mixed gendered ward or a single room.

Clinicians must also remain cognisant that patients may not be fully open about their gender identity with their family, friends or other members of the public. Where possible, this should be discussed

with patients to ascertain with whom they are happy for you to make reference to their gender identity with.

Gender dysphoria is a term that describes the sense of unease or psychological distress that a person may feel because of a mismatch between their sex assigned at birth and their gender identity. Clinicians must remain sensitive to the fact that interactions with a patient may enhance this distress. This distress may be stimulated if a patient is purposely withheld their hormone therapy for a prolonged period of time and they start to recognise changes not consistent with their gender identity. This can also happen, for example, in the context of chest binder removal. The negative effects of this dysphoria should not be underestimated and must be taken into consideration in patient-centred clinical decision making and caring for transgender patients.(28)

What are the next steps?

Education sits at the heart of progress. To date, the care of transgender patients is not included in FICM, RCoA or RCP curricula, despite the RCoA referencing articles on the subject in their care guidelines.(30) Undergraduate education on transgender healthcare is also poor, with only approximately 10% of medical schools including it in their curriculum.(31) There are also no national guidelines on the subject, despite multiple calls for their inception.

Our recent educational session for the Association of Anaesthetists demonstrated that clinicians' confidence in managing transgender patients can be significantly and rapidly increased.(6) Further work on the subject, its inclusion in undergraduate and postgraduate curriculums, ongoing training and the development of national guidelines are all likely to be key in driving transgender healthcare forward.

Conclusion

Transgender patients have several specific clinical and holistic considerations that are important to critical care clinicians. A baseline understanding of these is vital to allow optimal and safe care. Education on the subject both at an undergraduate and postgraduate level needs to improve, with the development of national guidelines likely a key step in the process.

Figure Legends:

Figure 1. *Specific considerations relevant to the care of transgender patients in critical care. CTM – cricothyroid membrane; HRT – hormone replacement therapy; ICU – intensive care unit; MDT – multidisciplinary team; VTE – venous thromboembolism*

Figure 2. *Endoscopic Glottoplasty in a transgender female. Images courtesy of Dr Paul Paddle.*

Figure 3 *i) Chest binding tape ii) Chest binder. Images used with permission from https://chestbinder.co/.*

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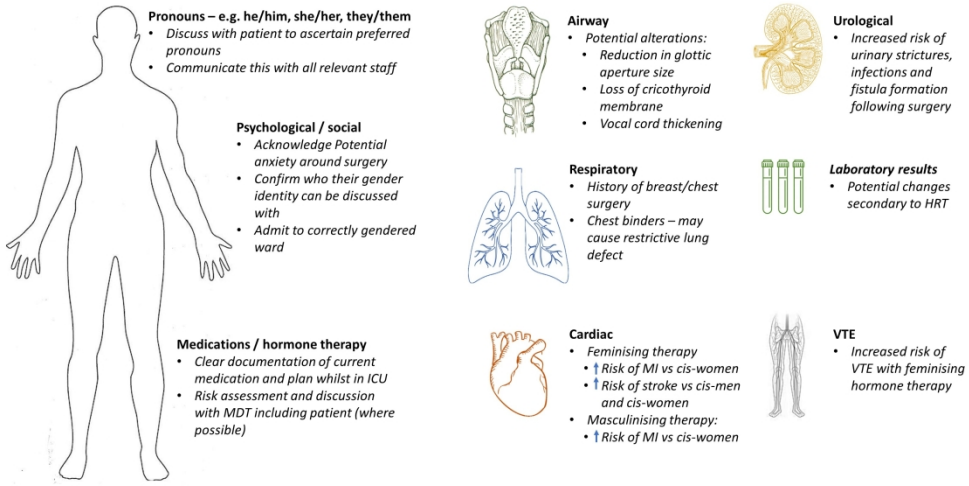

Figure 1. Specific considerations relevant to the care of transgender patients in critical care. CTM – cricothyroid membrane; HRT – hormone replacement therapy; ICU – intensive care unit; MDT – multidisciplinary team; VTE – venous thromboembolism

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