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REVIEW

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Central venous catheter use

Part 2: infectious complications

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Abstract Central venous catheters (CVCs) are used with increasing frequency in the intensive care unit and in general medical wards. Catheter infection, the most frequent complication of CVC use, is associated with increased morbidity, mortality, and duration of hospital stay. Risk factors in the development of catheter colonisation and bloodstream infection include patient factors (increased risk associated with malignancy, neutropenia, and shock) and treatment-related factors (increased risk associated with total parenteral nutrition, ICU admission for any reason, and endotracheal intubation). Other risk factors are prolonged catheter indwelling time, lack of asepsis during CVC insertion, and frequent manipulation of the catheter. The most important factor is catheter care after placement. Effects of CVC tunnelling on infection rates depend to a large extent on indwelling time and the quality of catheter care. Use of polyurethane dressings can increase the risk of colonisation compared to regular gauze dressing. Thrombus formation around the CVC tip increases the risk of infection; low-dose anticoagulants may decrease this risk. New developments such as CVC impregnation with antibiotics may reduce the risk of infection. Reducing catheter infection rates requires a multiple-strategy approach. Therefore, ICUs and other locations where CVCs are used should implement strict guidelines and protocols for catheter insertion, care, and maintenance.

Keywords Central venous catheter · Infectious complications · Catheter-related bacteraemia · Colonisation · Catheter-related sepsis · Preventive strategy · Literature review

Introduction

Central venous catheters (CVCs) are used in intensive care units (and, increasingly, in other locations) to administer intravenous fluids and blood products, drugs, parenteral nutrition, and to monitor haemodynamic status. The increasing morbidity and co-morbidity of ICU patients, duration of patient stay, and catheter indwelling time have led to an increase in CVC-related infections [1]. In addition, sicker patients are at higher risk of acquiring nosocomial infections including CVC infection [2]. All this has led to an increase in the occurrence of catheter-related infections (CRIs). These are associated with increased morbidity, mortality rates of 10–20% [3, 4, 5, 6, 7, 8], prolonged hospitalisation (mean: 7–14 days; survivors: 24 days), and increased medical costs estimated to be in excess of $10,000 per hospitalisation [3, 4, 5, 6, 7, 8]. The number of CRIs can be reduced by implementing a multiple-approach prevention strategy [9, 109]; this underscores the importance of an awareness of factors underlying CRIs, and the necessity of a rigorous protocol dealing with catheter care.

Mechanical complications of CVC use are discussed in Part 1 of this review. This article will focus on cathe-

ter-related infections, the most frequently occurring complication of CVC use. The risk of CVC infection increases if the insertion procedure was difficult [10, 11]. This is probably due to a higher risk of haematoma and thrombus formation which plays a central role in the development of catheter infection, as explained later.

Terms and definitions

A major source of confusion arises from inconsistent use of terms and definitions (Table 1). Thus the reported incidence of CVC-related infections varies from 1% to >40% [5, 8, 12, 13, 14, 15, 16]. This large variation is largely caused by differences in how CRI was defined. Terms such as 'clinical suspicion of catheter infection' are used without further explanation; 'catheter sepsis' usually does not mean the clinical syndrome of sepsis, but instead denotes catheter-related bactaeremia or catheter infection.

Comparisons are further complicated by differences in study design and patient populations. Important data regarding patient populations and catheter care may be missing. It is often unclear whether described patients were treated in an ICU or a general ward. Information regarding underlying disease and treatment is often not provided. Likewise, reasons for CVC use, indwelling time, number of CVC used concurrently, and whether medical and nursing staff had received proper training in catheter care are frequently not mentioned. This is relevant as all these factors are independently associated with an increased risk of CRI.

The term *'catheter infection'* has different meanings in the medical literature. It can signify clinical suspicion of catheter infection, but also a positive bacterial culture of a removed catheter segment, without clinical signs of infection. Another meaning is a positive blood culture drawn from the central line with 'suspicious' pathogens such as coagulase-negative staphylococci. There are no universally accepted definitions for catheter infection. The American Centers for Disease Control (CDC) have published definitions with relatively strict criteria for nosocomial infections, including CRIs [17]. According to these guidelines, CVC-related infection requires a combination of clinical signs of infection, a positive culture of blood aspirated from the catheter or of a catheter segment, and one or more positive blood cultures with the same pathogen taken from a different location. From the literature, clinical suspicion of catheter infection is confirmed in accordance with CDC criteria in approximately 20% of cases. These numbers are influenced by the accuracy of diagnostic test methods, especially culture techniques [18]. Most laboratories use the roll-plate method for culture of a CVC. This usually involves taking one segment of the catheter – usually the tip – then cutting it open and rolling it over a semi-solid medium. However, there is some evidence that this method may be inadequate [19]. Additional use of a different (liquid) culture media, culture of more than one catheter segment, and use of techniques such as sonication can increase both yield and culture sensitivity [20]. Correlation with catheter-related bactaeremia may also improve if more sophisticated methods are used [20]. Thus, results of cultures may be false negative; with clear clinical suspicion of a CRI, the catheter should be removed even if blood cultures are negative.

On the other hand, the catheter may be colonised at the time of extraction by bacteria present on the patient's skin at the insertion site, thus leading to false-positive culture results [21]. This may be problematic, especially when the organism cultured from the catheter tip after removal is commonly found on the skin, such as coagulase-negative staphylococcus. If a catheter is replaced over a guidewire because of a (low) clinical suspicion of infection, an erroneous conclusion that the old catheter was indeed infected may lead to unnecessary de novo insertion of a new catheter. Therefore, results of cultures from the catheter tip alone, without supporting evidence from other sources such as blood cultures, or a high index of clinical suspicion, should be interpreted with

Table 1 Terms and definitions

- *Catheter colonisation* or *catheter infection*: positive culture of a catheter segment[a]
- *Local infection*: clinical signs of infection at CVC insertion site (redness, pus) in combination with a positive culture from the skin and/or pus at the insertion site
- *Clinical suspicion of catheter infection:* one or more of the following: local infection; fever of unknown origin, with intravascular access device present for ≥3 days; positive blood cultures without clear focus of infection at other site; normalisation of temperature after CVC removal
- *Catheter-related bacteraemia*:[b] Clinical suspicion of infection (fever, chills, unexplained leukocytosis, hypotension, tachycardia etc) with no clear focus apart from the central line, *or* signs of local infection around the insertion site, *in combination with* a positive culture from a catheter segment and at least one positive blood culture with the same pathogen. The blood sample must be drawn from a different location (peripheral vein, arterial line, different central venous catheter) than from the potentially infected central line

[a] A potential problem in the interpretation of these results is that the catheter may be colonised from the skin during extraction [21]

[b] In many publications the term 'catheter-related sepsis' is used to describe catheter infection. In this context the term 'sepsis' usually means bacteraemia rather than the clinical syndrome of sepsis. This is confusing, and we prefer to use the term catheter related bacteraemia, reserving the term sepsis for the clinical syndrome

some caution. Catheters should not be replaced solely on the basis of the results of 'old' catheter tip cultures.

Pathophysiology and epidemiology

Catheter colonisation is a risk factor for catheter-related bacteraemia (CRB). Without colonisation there can be no catheter-related bacteraemia or 'catheter sepsis'. On the other hand, colonisation does not necessarily lead to CRB. This occurs in approximately 20% of cases [22], the risk depending on various factors described below.

Catheter colonisation is closely linked to the patient's skin flora, i.e., the types of bacteria found on the skin at the insertion site [23]. Thus, approximately 50% of catheter infections are caused by coagulase-negative staphylococci [22], but in CVCs inserted in the groin Gram-negative rods are the most common causes [23]. The risk of CRB increases if the insertion site was more heavily contaminated with bacteria prior to CVC insertion, irrespective of aseptic measures taken during the insertion procedure [22, 24]. The risk of infection is also linked to the number of bacteria present around the insertion site *after* CVC insertion [22]. In hospitalised patients, and especially in the ICU, the 'normal' skin flora is likely to be (partly) replaced by more pathogenic and/or more resistant bacteria, reflecting the hospital as opposed to the home environment. Furthermore, local circumstances at the insertion site (warm, moist, presence of corpus alienus) are generally advantageous for bacterial growth.

A key event in bacterial colonisation of the CVC is *thrombus formation*. The risk of infection is increased dramatically by thrombus formation around the catheter tip [8, 25, 26]. The thrombus probably serves as culture medium for bacteria, allowing them to multiply more rapidly and easily. Thrombus formation around the catheter tip or at the site where the CVC penetrates the vessel wall occurs frequently, in 33–67% of patients when the CVC indwelling time exceeds one week [26, 27, 28]. Apart from the thrombogenicity of the catheter material, the risk of subsequent thrombus formation is also determined by the extent of damage to the vascular wall occurring during insertion [29].

Thus, the pathogenesis of 'catheter sepsis' is probably as follows. The first step is catheter colonisation by bacteria from the skin surrounding the insertion site. The more bacteria present near the site, the greater the risk and speed of colonisation. This colonisation may occur immediately, during the insertion procedure, or at any time subsequently. In the latter case, colonisation and survival of the bacteria in or on the catheter is facilitated if a thrombus has formed at the catheter tip or at the site where the CVC penetrates the vessel wall. Once colonisation has occurred and bacteria have taken hold in or on the CVC, catheter-related bacteraemia can occur depending on various circumstances. Only a small proportion of infections arise from 'external' sources such as contaminated infusion fluids. However, bacteria can easily be transferred from the skin of one patient to another by medical and nursing staff, and this may result in catheter colonisation by (resistant) bacteria. Hygiene measures (hand-washing by medical and nursing staff, use of alcohol dispensers, etc.) play an important role in preventing catheter colonisation. In addition, the patient's skin flora and number of bacteria can be influenced by (lack of) hygiene; this can lead to replacement of the patient's own skin flora by bacteria with greater resistance to antibiotics.

Factors determining risk of infection

Underlying disease

The patient's primary diagnosis and co-morbidity influence the risk of CRI [30, 31, 32, 33, 34]. This correlation is most evident in patients with neutropenia and/or receiving immunosuppressive therapy with the exception of corticosteroids [33, 34]. Malignancy and hyperalimentation also increase the risk of CRI. Parenteral feeding is also a significant risk factor [35, 36], probably because it can lead to precipitation of feed in stopcocks, valves, and in the line itself. This is especially so when the same lumen is used to administer other products or medication [37]. Parenteral feed is an excellent culture medium for bacteria. In addition, use of the CVC for parenteral feeding may lead to increased use and decreased hygiene during CVC manipulation.

Increased risk for CVC infection has also been linked to exposure of the catheter to remote-source bacteria [1, 23], and in those patients with lower respiratory tract infection or colonisation [38], or active urinary tract infection [39]. No clear increase in the risk for CRI has been demonstrated for diabetes, treatment with corticosteroids and a history of infection longer than 48 h prior to CVC insertion; however, these factors may increase the risk of catheter colonisation leading to CRB.

Other clinical factors

Risk factor analysis based on prospectively collected data and the use of multivariate analysis have shown that the risk of developing nosocomial infections (including CVC infection) is linked to ICU admission, mechanical ventilation, invasive haemodynamic monitoring, and any type of shock (including non-distributive shock) [1, 22]. Each of these factors appears to increase the risk of infection by a factor of about 2–2.5 [1, 23].

Catheter types and materials

CVCs can be divided into tunnelled (Hickman, Groshong, Portacath) and non-tunnelled catheters, with 1–4 lumens. Use of multi-lumen catheters may be associated with a slightly increased risk of infection [8, 40, 41, 42]. However, this may be due in part to more intensive use and more frequent manipulations of the catheter. The most frequently used materials are silicone, polyurethane, polyvinylchloride, polypropylene, and Teflon. Differences between these materials are mainly mechanical (see part 1 of this review for more extensive discussion). Differences in thrombogenicity may influence the risk of infection.

If a long indwelling time is expected, *tunnelling* of the CVC is an option to decrease the risk of infection. A recent meta-analysis found a small benefit of tunnelling in CVCs inserted in the jugular vein, but not in the subclavian vein [43]. The potential advantages of tunnelling do depend to a substantial degree on other factors such as catheter use, care, and maintenance [8]. Two controlled trials [44, 45] have reported that non-cuffed tunnelled and non-tunnelled catheters have similar infection rates in short-term use if strict infection control practices are adhered to.

Tunnelling is valuable in situations where catheter care is not optimal (treatment in the home setting, wards with little experience in catheter care), or in situations where the risk of colonisation is high (proximity of insertion site to tracheostomy, burn wound, skin laceration or other potential source of infection [46]). Tunnelling is also required as a site for the anchorage cuffs of Hickman lines and other implant devices. If nursing care and maintenance of the catheter are optimal, differences in infection risk are minor or absent [43, 44, 47]. Thus, CVC tunnelling is not required in the ICU setting, except perhaps in situations where a (very) long indwelling time is to be expected. Benefits of tunnelling may be somewhat greater if the CVC is located in the jugular vein.

The risk of catheter infection appears to be significantly higher in catheters used for long-term haemodialysis [48, 49]. In this category of catheters with very long indwelling time, tunnelling may increase the life span of the catheter and decrease the incidence of CRB [50].

Insertion procedure

The number of bacteria present on the skin at or near the insertion site is closely linked to the subsequent risk of infection [1, 24]. The risk of infection increases considerably if insertion takes place in emergency situations with suboptimal sterile field preparation. Such catheters should be removed or replaced within 24 h.

Various studies have investigated the degree of asepsis needed during CVC insertion. Although some reported that a sterile procedure (hand washing, mask, cap, sterile gloves and field) may be sufficient [8, 51, 52], others concluded that more strict asepsis using maximum sterile barrier precautions (sterile scrub, caps, mask, sterile surgical gown, gloves, and large drapes) can significantly reduce infection risks [53, 54]. It seems likely that patient factors such as neutropenia [53] and operator experience are important in this regard. Although there is no conclusive evidence, we recommend erring on the side of caution and applying strict aseptic procedures (i.e., maximum barrier precaution) during routine CVC insertion. Chlorhexidine (rather than iodine or alcohol) should be the preferred method for skin disinfection, as this has been shown to be superior in preventing CRIs [55]. Acetone should not be used [8].

Choice of insertion site

The risk of infection in the medium- and long term is highest for the femoral vein, lower for the jugular vein, and lowest for the subclavian vein [56, 57, 58]. This is probably due to the greater degree of bacterial colonisation of the groin compared to the shoulder and neck [56, 57]. The types of bacteria causing CRIs also differ (groin: greater frequency of *Enterococci*, *Enterobacteria*, *Pseudomonas* species, and other Gram-negative rods; shoulder/neck: mostly coagulase-negative *Staphylococci*). When selecting the insertion site, it should be remembered that mechanical complications, difficult insertion procedures, and altered local anatomy (for example, a medical history of sternotomy or clavicular fracture) is associated with a higher risk of complications and malpositioning. The complication risk also increases if CVCs have previously been placed at the chosen site of insertion. This is probably due to the high incidence of (usually asymptomatic) venous thrombosis at these sites [26, 59]. We suggest the subclavian approach as first choice when a long indwelling time (≥1 week) is anticipated. As jugular vein insertion may carry a lower risk of mechanical complications (especially pneumothorax), this approach may be preferred if a short indwelling time is expected. For a more extensive discussion of insertion sites, see Part 1 of this review.

Indwelling time

There is a strong correlation between catheter indwelling time and risk of infection. If indwelling time is less than 3 days the risk of CRB is virtually zero. If indwelling time is 3–7 days this risk increases to between 3–5%. If indwelling time is more than 7 days, the cumulative risk increases to 5–10% [5, 8, 16, 23].

Catheter care

Appropriate care of the catheter and insertion site plays a crucial role in reducing the risk of infection and CRB. One study designed to assess the effect of tunnelling on infection risk did initially observe a significant difference between tunnelled and non-tunnelled CVCs. However, when care and maintenance of non-tunnelled CVCs was taken over by specialised nurses, and a strict protocol regarding catheter care and hygiene was implemented, the difference in infection risk disappeared [44]. Overall infection risk, even for tunnelled catheters, also decreased with the improvements in nursing care [44]. More recent studies confirm the highly significant decreases in infection risk by a multiple-approach prevention strategy targeted at insertion and maintenance of vascular access devices [9, 60].

Hygienic measures such as hand washing and use of hand alcohol should be implemented before any use of the CVC. Injection ports should be cleaned with chlorhexidine, iodine or 70% alcohol before and after accessing the system. Various studies have found that infusion systems attached to the CVC (especially stopcocks and catheter hubs) frequently become colonised (approximately 50% within 3 days) [8, 61, 62]. Therefore, the infusion system, including piggyback tubing and stopcocks, should be changed every 48–72 h under aseptic conditions [63]. More frequent changes convey no extra benefit [63], although earlier change may be warranted in case of contamination, frequent and intensive use of the system (drawing blood samples, frequent intermittent administration of medication), and/or if lipids or blood products have been administered through the line.

Dressing and care of the insertion site

Transparent, semipermeable, polyurethane dressings have become a popular means of dressing catheter insertion sites. Their advantages are that they permit continuous visual inspection of the catheter site and require less frequent changes than do standard gauze and tape dressings, thus saving personnel time. In addition, ambulant patients with CVCs secured with transparent dressings are able to bathe and shower without saturating the dressing. However, the use of these dressings is controversial: a number of studies comparing transparent polyurethane dressings to sterile gauze have reported that the former may increase microbial colonisation and risk of subsequent CRB [64, 65, 66, 67, 68, 69]. In a meta-analysis of catheter dressing regimens, CVCs on which a transparent dressing was used had a significantly higher incidence of catheter-tip colonisation and a non-significant trend towards a higher incidence of CRB [70].

On the other hand, the observed differences are often quite small. Other investigators have reported no or only minor differences in catheter colonisation and infection [71, 72, 73]. The higher incidence of colonisation may be due, in part, to differences in catheter care; for example, if gauze becomes soiled or wet it may be changed more quickly than when small collections of fluid or blood develop under a transparent film. This may facilitate growth of bacteria and CVC colonisation. Some investigators have reported that newer transparent dressings that permit the escape of moisture from beneath the dressing may have somewhat lower rates of skin colonisation and CRI [74, 75]. However, others have found no differences between these new dressings and ‘traditional’ film dressings such as Tegaderm [76, 77].

Overall, the potential risk of colonisation and infection associated with transparent polyurethane dressings appears to be at least equal and probably (slightly) higher than for sterile gauze dressing. Therefore, we recommend the use of sterile gauze rather than transparent dressing in most situations. Exceptions may be the presence of open wounds or a tracheostomy near the insertion site, the necessity for extra fixation of the CVC, or dribbling of large amounts of saliva from the mouth (for example, in patients with neurological injury or disease) which may contaminate the CVC if it is located in the neck or shoulder. Insertion site dressings should be changed at least every 48 h, and earlier if they become soiled or wet. When the gauze is changed the insertion site should be cleaned with alcohol or chlorhexidine, and inspected carefully for signs of infection (erythema>1 cm, tenderness, induration and/or exudate around site, pus). If polyurethane dressings are used, we recommend that these also be changed at least every 48 h, and/or whenever a collection of fluid or blood/thrombus is visible around the insertion site. It should be kept in mind that most catheters contain chemical additives. These can leak into the surrounding skin (especially if the indwelling time is long), and cause local (chemical) inflammation, which may be difficult to distinguish from bacterial infection. Pus exuding from the insertion site always indicates (bacterial or fungal) infection.

Impregnation with antiseptics or antibiotics

A fairly recent development is the use of CVCs impregnated with antiseptics or antibiotics to prevent catheter colonisation and subsequent CRB. A substantial number of in vivo and in vitro studies have been carried out in recent years to test the efficacy and cost-effectiveness of these catheters. Most studies have reported modest to substantial decreases in catheter infection rates [78, 79, 80, 81, 82, 83, 84]. Impregnation with antiseptics (usually chlorhexidine and sulphadiazine) appears to decrease the risk of catheter colonisation [78, 80], although the effect on CRB is less clear [80]. Analytic models using research data, meta-analyses and safety data from the US

Food and Drug Administration have suggested that use of these devices would be cost-effective in patients at high risk for CRB [84]. Attempts have also been made to prevent catheter colonisation through positioning of antiseptic-impregnated cuffs at the skin exit site; however, the results have been disappointing [110, 111].

Studies dealing with CVCs impregnated with antibiotics (usually rifampicin and minocycline) have reported highly significant decreases (50–70%) in both CVC colonisation and CRB [81, 82]. In a recent study directly comparing CVCs impregnated with antiseptics to CVCs impregnated with antibiotics [83], catheters impregnated with minocycline and rifampin were one third as likely to be colonised as catheters impregnated with chlorhexidine and silver sulphadiazine. The rates of CRB were 3.4% vs 0.3% [81]. In vitro studies have confirmed that resistance to bacterial colonisation of CVCs impregnated with antibiotics may be superior to CVCs impregnated with antiseptics [83].

A potentially serious risk is the induction of antibiotic resistance by the use of these catheters. However, no evidence has yet been found of this occurring, even after long-term use on a routine basis. In addition, if reduction of infections could be achieved by utilising these CVCs, the systemic use of antibiotics might decrease, thus helping to reduce antibiotic resistance. Another potential drawback of these catheters is the additional cost incurred, currently 2–3 times that of 'regular' multi-lumen CVCs. However, if decreases in the incidence of CRI comparable to those reported in the literature could be brought about, reductions in costs achieved by shorter hospital stay would almost certainly make the new CVCs cost-effective if used in selected patients.

No data are currently available regarding possible allergic or anaphylactic reactions to CVCs impregnated with antibiotics. Some cases of anaphylactic reactions induced by antiseptic-impregnated catheters have been reported in the literature, mostly in Japan but, recently, also in Europe [112].

Flush solutions and anticoagulants

Thrombus formation at the catheter tip or at the site where the catheter penetrates the vessel wall plays a role in facilitating catheter colonisation and subsequent CRB [25, 26]. Thus it seems logical to assume that prevention of thrombus formation might also decrease the risk of CRI. Various investigators have reported that the risk of catheter infection is indeed decreased by intravenous administration of heparin or by flushing with heparin solution [28, 85]. Others have reported decreased risk of CRI associated with the use of low doses of oral anticoagulants [86, 87], and possibly even subcutaneous low-molecular weight heparin [88]. However, this applies only if administration of anticoagulants begins immediately after the CVC is inserted; administration of anticoagulants after a septic thrombus has already formed can cause septic embolism through detachment of infected parts of the thrombus. Apart from bleeding complications it should be remembered that heparin, even in low-dose flush solutions [89, 90], can cause heparin-induced thrombocytopenia (HIT). Many manufactures of central lines put a heparin coating on the CVC, although the effectiveness of this has not been established; most commercially available pulmonary artery catheters are heparin-coated. Such heparin coating can also induce HIT [91], and is likely to be overlooked when searching for the cause of thrombocytopenia. The incidence of HIT induced solely by heparin coating has been reported to be 0.4% [91].

Other preventive strategies and future developments

Inline bacterial filters may reduce the incidence of phlebitis in peripheral lines, but studies regarding their effect on preventing CRI have proved disappointing. A more recent development is the use of *electric current* in silver ionotrophic catheters to prevent bacterial colonisation [92]. This involves wrapping an electrically charged (usually 1.5 V, 20 μA) pair of silver wires helically around the catheter. This produces a continuous release of silver ions that inhibit bacterial growth. The electric field itself may also have a direct antibacterial effect [92]. However, although tests in vitro and in an animal model seem promising [92], there are as yet no clinical trials involving these catheters.

Another approach is the study of mechanisms by which bacteria such as *S. epidermidis* and *S. aureus* can attach themselves to CVCs, and developing methods to prevent this adherence [93, 94]. Coating future catheters with specific anti-adhesion molecules may help prevent CRI.

Yet another potential future development is inhibition of biofilm formation by targeting bacterial intercellular signal molecules. Biofilm formation is an important step in catheter colonisation by, for example, *P. aeruginosa*; thus inhibition of this process could help prevent colonisation and CRI by various bacterial species including Pseudomonas.

Routine (elective) catheter replacement

The practice of routine replacement of CVCs, i.e., replacement in the absence of clinical signs of infection, is still common practice in many centres. The reason for this is the clear correlation between catheter indwelling time and the risk of infection [5, 8, 16, 23]. This practice has been evaluated in several clinical trials, most of which used the procedure of guidewire exchange to re-

place the catheter. Studies in which CVCs were replaced every 3 days or 7 days reported no decrease in infection rates [13, 95]; indeed, the risk of infection appeared to be *increased* by this procedure [13]. Moreover, morbidity due to mechanical complications was increased [13, 95]. De novo replacement at 7 days also did not reduce infection rates [96]. Thus, there is currently no evidence to support the practice of routine de novo or guidewire exchange when clinical signs of infection are absent.

Special situations and procedures

Guidewire exchange

When CRI is suspected many clinicians prefer to replace the catheter by guidewire exchange. This entails the removal of a catheter over a guidewire followed by its replacement at the same insertion site. A segment of the original catheter is cultured and the new catheter removed if these cultures are positive. This strategy is used to reduce the risk of mechanical complications associated with de novo CVC insertion [13, 97]. However, although widely used this strategy is controversial. Some investigators have reported increases in CRB associated with this procedure [13]; in a meta-analysis of 12 randomised controlled trials, guidewire exchange appeared to be associated with a greater risk of catheter colonisation and CRI, but fewer mechanical complications than new site replacement [98]. However, the differences in this meta-analysis were not statistically significant, and others have found no such increase provided very strict criteria for guidewire exchange were applied [95, 97, 99].

The question of if and when to use guidewire exchange has not been conclusively settled. We recommend the following approach: if there is clinical suspicion of catheter infection and there are no serious contraindications for CVC insertion (see Part 1 of this review), the catheter should be removed and a new one inserted de novo. Careful evaluation should take place daily as to the clinical indications for the CVC; all CVCs should be removed at the earliest possible opportunity. Guidewire exchange should be considered if: (i) insertion of a new CVC is likely to pose significant risks to the patient and/or severe technical problems are likely to be encountered during insertion; or (ii) suspicion of CVC infection is not high, but cannot be excluded with certainty (for example, a patient with fever where there is an alternative source of infection, with no clear signs of CVC infection, but a line which has been in situ for more than a week). The catheter should always be cultured after removal. If the culture is positive the new catheter should be removed and de novo insertion should take place. If possible the 'old' line should be removed prior to insertion of the 'new' line. If this is not possible (for example, if the patient requires continuous vasoactive medication), antibiotic prophylaxis may be considered prior to insertion of the new line. In our opinion, if the insertion procedure of the new line was uncomplicated, the old line should be removed as quickly as possible, without waiting for an X-ray to confirm the new catheter's position.

Pulmonary artery (Swan-Ganz) catheters

The pathophysiologic principles outlined above also apply to pulmonary artery catheters (PACs). Indications and use of PACs are currently being debated, with some reports suggesting that PACs are often overused and/or associated with increased morbidity and mortality; however, this discussion will not be dealt with here. Once a PAC has been inserted, colonisation and infection occurs in the same way, and risk factors are the same as outlined above for 'regular' CVCs. As with regular CVCs, infection rates are very low in the first 3 days after placement, after which the risks increase significantly [100, 101, 102]. However, morbidity and mortality associated with PAC infection are much higher, due to the fact that PAC infection may lead immediately to endocarditis. Therefore, we strongly recommend removing or exchanging PACs after 72–96 h. Replacement should be accomplished by de novo insertion and not by guidewire exchange. For a more extensive discussion of the pathogenesis and epidemiology of PAC infection, see the quoted review [103].

Antibiotic prophylaxis

In some centres it is customary to administer a short course (24 h or less) of antibiotics prophylactically when CVCs are inserted or replaced. Studies dealing with the effectiveness of this practice have produced conflicting results [85, 104, 105, 106, 107, 108]; however, most studies show that a modest decrease in CVC infection rate may be achieved through antibiotic prophylaxis [104, 105, 106, 107]. Whether this advantage outweighs potential risks such as induction of antibiotic resistance is unclear. Moreover, CVC impregnation with antibiotics may be a more effective way of preventing infection through antibiotic prophylaxis [81, 82] with less risk of antibiotic resistance. In practice, many patients admitted to the ICU already receive antibiotic prophylaxis following surgical procedures.

Many centres also use antibiotic prophylaxis, usually a single dose of vancomycin, when a catheter is replaced on suspicion of CVC infection. So far, no controlled studies have been carried out to assess the effectiveness of this practice. Potential side effects of vancomycin such as induction of hypotension and the 'red man syndrome', as well as concerns regarding antibiotic resistance, may limit its application for this purpose.

Table 2 Protocol for the choice of insertion site, insertion procedure, and catheter care and maintenance for indwelling central venous catheters in the ICU

I. CVC insertion

1. Select appropriate catheter: as few lumens and as soft material as possible; (see Tables 1 & 2, Part 1 of this review). Catheter should not be too long; tip should be located in vena cava
2. Consider use of impregnated catheters in high-risk patients. Consider tunnelling if very long indwelling time is expected, or unit has little experience in catheter care
3. Select the appropriate site, taking into account:
   - The patient's medical history and other clinical factors (see Table 3, Part 1 of this review)
   - Whether CVCs were previously inserted at the same site (this increases the risk of mechanical complications and subsequent CRI)
   - Expected CVC indwelling time (if >1 week, select subclavian vein if possible)
   - Purpose of CVC
   - Personal preference and experience of physician performing the insertion procedure
4. Use aseptic insertion procedure: sterile scrub, caps, mask, sterile surgical gown, gloves, and large drapes. Disinfect skin using chlorhexidine rather than iodine or alcohol
5. Remove lines as quickly as possible if not inserted under strict aseptic conditions
6. Limit insertion attempts of inexperienced doctors to two

II. Care of insertion site

7. Use sterile gauze rather than polyurethane dressings to cover insertion site (exceptions: see section dealing with *Dressing and care of the insertion site* in Part 2 of this review. Change dressing (gauze or polyurethane) every 24–48 h, or earlier if soiled. Inspect insertion site for signs of local infection. Change infusion system every 72 h
8. Apply strict handwashing and/or rinsing with alcohol before every catheter manipulation. Clean stopcocks with alcohol or chlorhexidine after every manipulation
9. Consider use of low-dose anticoagulants. Do not use local antibiotics

III. Suspicion of CRB

10. Remove catheter if there are definite signs of local infection (pus, area of redness ≥2 cm). Remove catheter if CRI is suspected. If catheter is still required: de novo insertion, preferably at different site
    Consider guidewire exchange if there are clear contra-indications for de novo insertion. Culture catheter segment; if positive, remove the replacement catheter
11. Risk of CRB is higher if insertion procedure was difficult, or if mechanical complications have occurred during insertion

Conclusions

Catheter infection and catheter-related bacteraemia are the most serious and frequently occurring complications of CVC use, carrying a high morbidity and mortality, and increasing the costs of medical treatment and length of hospitalisation. The risk of infection increases especially when indwelling time is long (>7 days). The most important preventive measures are strict asepsis during insertion, and during catheter care and maintenance. CVC tunnelling decreases the infection risk mainly in situations where catheter care is suboptimal, or when a very long indwelling time (weeks–months) is anticipated. Catheter impregnation with antibiotics appears promising, and may be one way of decreasing infection rates. Further evaluation of benefits and risks (especially induction of antibiotic resistance) of these catheters is required. Other potential future developments include use of electrically charged catheters and application of genetic and molecular technology to prevent bacterial adhesion and biofilm formation. All hospitals and ICUs using CVCs should develop protocols and strict guidelines regarding catheter insertion, catheter care and maintenance, and procedures for situations where catheter infection is suspected. Implementation of such protocols can significantly reduce morbidity and mortality associated with CVC infection. A brief protocol for the insertion and maintenance of central venous catheters, based on the data from this review and our review dealing with mechanical complications, is provided in Table 2.

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