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A comparison of the risk factors and complications associated with peripherally inserted central catheter (PICC) and totally implantable venous access port (TIVAP) usage in cancer patients

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Abstract

This literature review discusses and compares the risk factors and complications associated with using peripherally inserted central catheters (PICCs) and totally implantable venous access ports (TIVAPs), particularly for cancer patients. Research related to this topic from within the last 10 years was found and reviewed. Major PICC complications identified include phlebitis, thrombosis, infections, occlusion and mechanical problems. The independent risk factors that correlate with these include drinking, prior surgery history and immunotherapy. Drinking correlated with phlebitis and thrombosis, whereas prior surgery history correlated with thrombosis, occlusion and mechanical complications. Major TIVAP complications identified include mechanical issues, infection and occlusion. The risk factors associated with these include age, type of cancer, and adjuvant versus non-adjuvant chemotherapy treatments. Haematological head and neck, and gynecological cancers were associated with higher risk of infection. Adjuvant settings had lower risks of infection. Overall, TIVAPs were found to have a lower incidence of venous access device related complications compared to PICCs.

Keywords: peripherally inserted central catheter (PICC); totally implantable venous access port (TIVAP); cancer; risk factors; complications

Introduction

Peripherally inserted central catheters (PICCs) are long, thin central venous access devices used to allow medical practitioners access to veins in order to administer medicines, such as chemotherapy, immunotherapy and other targeted therapy drugs (Liu et al., 2015). They are commonly inserted in a peripheral upper arm vein, such as the basilic or brachial vein (Mielke et al., 2020). PICCs facilitate both in-patient and out-patient chemotherapy, and are accepted as convenient and accessible devices used in oncology departments.

Totally implantable venous access ports (TIVAPs) are also venous access devices used frequently for chemotherapy, blood transfusions, and other medical purposes (Yu et al., 2018). Unlike PICCs, these devices are composed of an injection port implanted into the subcutaneous tissue, and a central venous catheter fed into the blood vessel. One of the major advantages of TIVAPs is that they allow for patient activity, as they need no external dressing, and the

necessary maintenance for them is infrequent (often only monthly).

Although both devices have their merits, there are complications that arise through their usage. Awareness of the risks factors and complications of these venous access devices is crucial to maintain quality of patient care for oncology patients, amongst others. The devices can be compared to determine their suitability for said patients.

The aim of this review is to compare and contrast the risk factors associated with complications that emerge from the applications of PICCs and TIVAPs. This may further assess which device is more suitable for cancer treatments, and/or reveal further areas of investigation related to the study. The study will outline the risk factors that correlate most significantly with the respective complications for each type of device, then use the comparison of these results, along with previous research that have compared the two devices, to draw conclusions on their effectiveness and identify future potential areas of study.

Focusing this study on cancer patients allows for a better comparison between these two devices, as they are both commonly used in chemotherapy. The literature being reviewed and compared are by Cao et al. (2020), Mielke et al. (2020), Yu et al. (2018), Wang et al. (2015), Bassi et al (2012), Taxbro et al (2019), and Akhtar and Lee (2021). These papers were found and selected when searching for open-access research related to PICC and TIVAP related risk factors and complications in cancer patients, with the search limited to papers within the last 10 years (2011-2021) in order to account for the most recent findings available.

1. Risk Factors for Peripherally Inserted Central Catheters (PICC)

Drinking

In a retrospective study, Cao et al. (2020) identified that one of the major independent risk factors increasing PICC-related complications was drinking. Drinking was associated with high blood pressure and increased negative impacts on vascular health, explaining its correlation with increased incidence of complications. (Cao et al., 2020)

Prior Surgery History

Cao et al. (2020) also identified prior surgery history as a significant risk factor. Regarding why prior surgery history may have correlated with complications, given that the majority of the patients in their study had malignancies, Cao et al. (2020) stated that the patients' health would have further declined as they had undergone operations before PICC insertion.

Immunotherapy

Immunotherapy is a form of cancer treatment that enhances the body's immune system by allowing it to identify, target, and eliminate cancer cells. (Cancer Research Institute 2016). This differs from chemotherapy, which acts directly on the body's cancerous tumours. Mielke et al. (2020) found that for oncological treatment, only immunotherapy could be identified as an independent risk factor for complications when utilising PICCs, particularly correlating with local skin complications.

Type of Cancer

Mielke et al. (2020) also identified specific risk factors that contributed to thrombotic events— namely, how different cancer entities corresponded with rates of thrombosis event occurrences. The highest rates of thrombotic event occurrences were observed in tumours of the pancreas, brain and stomach.

Diameter of Catheter

Mielke et al. (2020) highlighted that the diameter of the catheter used (i.e. the lumen size) was a significant factor to consider in relation to thrombotic events. They found that double lumen PICCs were sufficient for the patients in their study.

Other Risk Factors

Other factors such as the insertion site of the PICC line, age —which is consistent with other studies (Shi et al., 2014) — and smoking were also identified by Cao et al. (2020). However, it was determined that while such factors impacted one of the PICC-related complications

(in the case of insertion site, for instance, this would be mechanical complications), they did not have a significant impact on total PICC related complications. (Cao et al., 2020)

Risk factors identified in other studies that were not explicitly included in the studies by Cao et al. (2020) and Mielke et al. (2020) include age, BMI, and low levels of physical activity. These correlated with the risk of thrombosis in cancer patients. (Al-Asadi et al., 2019) (Shi et al. 2014) (Liu et al., 2015)

2. Complications for Peripherally Inserted Central Catheters (PICC)

Vascular Complications

Cao et al. (2020) found that the complications with the highest incidence were vascular complications such as phlebitis (inflammation of the innermost layer of the vein) and thrombosis (blood clotting in the vessel). The risk factor drinking correlated with increased phlebitis and thrombosis. They found that alcohol consumption led to adverse effects on patients' blood vessels, explaining vascular complications previously stated (Cao et al., 2020).

Similarly, Mielke et al. (2020) identified local inflammation, deep vein thrombosis, and occlusion (blockage of the vessel) as complications associated with PICC use. They found that patients receiving immunotherapy developed local inflammation at the catheter exit site (Mielke et al., 2020). The highest incidence of catheter related thrombosis was found in critically ill patients, individuals with prior thrombotic events, active tumour disease and systemic inflammation. All of these were present in their patients. (Mielke et al., 2020)

They identified that in the treatment of various cancers, the radiation beam used itself could have had thrombogenic effects, however, it was not clear whether or not these thrombogenic factors resulted in a higher rate of PICC-related thrombosis for their patient group specifically. (Mielke et al., 2020)

Infection

The study by Cao et al. (2020) also included infections as a high frequency complication, diagnosed if the patient was presenting and growing a pathogenic organism. To justify why prior surgeries may have correlated with infections (as well as phlebitis and mechanical problems), Cao et al. (2020) explained that malignancies were very consumptive diseases that often required prior surgery. The nature of these diseases and surgeries would have had an effect on these complications.

In the study by Mielke et al. (2020), bloodstream infections were another significant complication, found to have occurred less frequently in out-patient settings compared to in-patient settings.

Other Complications

Aside from the complications discussed above, bleeding and mechanical complications were also identified as potential complications of PICC use. (Cao et al., 2020)

3. Evaluation of the Studies (PICC)

Cao et al. (2020) do not consider lumen size of the PICC lines used, as they were unable to collect the relevant data for this, whereas Mielke et al. (2020) identified that the incidence of thrombosis increases depending on the diameter of the lumen, and considered this to reason why their use of double lumen PICCs were sufficient for their patients. This omitted variable may have adversely impacted the results in the study conducted by Cao et al. (2020).

Both studies performed were retrospective analyses (identifying trends and patterns in information that had already been collected from the past). Retrospective studies make use of convenience sampling when collecting data, and therefore by nature, are liable to bias. They also lend themselves to more correlation-based relationships, rather than causational. Given this, it could be argued that in the study by Cao et al. (2020), there is no certainty that there is a causal relationship between the risk factors identified—the relationship thus far can only be said to be correlation-based.

Additionally, Cao et al. (2020) included 4959 patients in their study, a much higher

sample size compared to the study by Mielke et al. (2020), which included 488 patients. Cao et al. (2020) also performed their investigation on multiple centres, whereas Mielke et al. (2020) conducted a single-centre study. Given that the sample size used by Mielke et al. was much smaller than Cao et al. (2020), this may indicate that the latter has more representative data and conclusions to offer.

However, Mielke et al. (2020) focused their study primarily on oncological patients, whereas Cao et al. (2020) performed their study on patients with PICCs regardless of the demographic, medican status or indications of patients (although they did find that the majority of their patients had malignancies). This may explain why the sample size in the study by Cao et al. (2020) is much larger, and suggests that their data may not be specific enough to be applicable to cancer patients.

In summary, although Cao et al. (2020) had access to more information and representative data for the use of PICC in general, Mielke et al. (2020) concluded findings specifically applicable to oncology patients.

4. Risk Factors for Totally Implantable Venous Access Ports (TIVAP)

Cancer Entity

In a study by Yu et al. (2018), type of cancer entity was distinguished as a significant risk factor for late complications in the use of TIVAPs. Patients with breast cancer, lung cancer and gastric cancer had higher rates of complication incidence compared to other malignancies, and this may be attributed to the fact that patients with these cancers had a higher indwelling time of the TIVAP. (Yu et al. 2018). Whilst this was consistent with the study by Wang et al. (2015), in which the site of the malignancy was also significant, they identified different cancer entities with higher complication incidence rates. Patients with haematological, head and neck, and gynecological cancers were found to be more prone to infections compared to other cancers. (Wang et al., 2015) Contributing factors to this for haematological cancers include neutropenia (low concentration of a specific type of white blood cell—neutrophils), immunosuppression and frequent catheter manipulations (Mollee et al., 2011).

Age

Whilst Yu et al. (2018) suggested age as another significant risk factor, it was not determined to be significant in the study by Wang et al. (2020). The relationship between age and complication incidence was determined to be most likely due to vascular changes that come with ageing. (Yu et al. 2018).

Chemotherapy Setting

Wang et al. (2015) found that chemotherapy setting was another significant risk factor for TIVAP use. TIVAPs used in adjuvant chemotherapy (therapy given to patients in addition to the initial treatment in order to maximise its effectiveness) versus non-adjuvant chemotherapy had a lower risk of infection. This may be because in adjuvant settings, patients are often in early stages of the tumour, and as a result fewer hospitalisations occur. (Wang et al., 2015)

Other Risk Factors

Yu et al. (2018) also used statistical analysis to investigate whether or not sex and site of TIVAP insertion correlated with increased complication rates. They found that these were not significant risk factors. This is consistent with other studies. (Wang et al. 2015) (Nagasawa et al., 2014)

5. Complications for Totally Implantable Venous Access Ports (TIVAP)

Mechanical Issues

Yu et al. (2018) determined that mechanical issues in TIVAPs were the most common complication that occurred. Similarly, a study by Bassi et al. (2012) identified the most common complication to be catheter malfunction. Catheter malfunction impeded the use of the port for patients.

Infection

Infections followed mechanical issues as a high incidence complication in the study by Yu et al. (2018). Local infection of the tissue at the site of venous access as well as catheter-related

bloodstream infection were both present. This was consistent with the study by Bassi et al. (2012). In their study, infections included catheter-related bloodstream infection and local infection of the site of venous access. Local infections included infection at the site of needle puncture, and pocket infections in the subcutaneous pocket of the TIVAP.

Vascular Complications

For patients with a long-term indwelling of the TIVAP, there were also catheter obstruction related complications. Two types of catheter obstructions were identified— thrombotic and non thrombotic (e.g. physical distortion of the catheter), and complications arising from these included slow catheter infusion and failure to transfuse or draw back blood. (Yu et al., 2018). Bassi et al. (2012) identified occlusion as another complication too, including withdrawal occlusion (occlusion where fluid can be pushed in but blood cannot aspirate).

6. Evaluation of the Studies (TIVAPs)

All three studies outlined above were conducted retrospectively. As previously mentioned, retrospective studies are often subject to bias by nature. Furthermore, the studies by Yu et al. (2018) and Bassi et al. (2012) both had a significantly lower sample size of patients compared to Wang et al. (2015), with 500, 81 and 1391 patients respectively. This reduces the statistical power of their findings. Yu et al. (2018) also focused their study on just late complications of TIVAP use, which, along with their low sample size, would have further contributed to sampling bias. Bassi et al. (2012) had a particularly small number of patients, which may have inflated the statistical results they provided for the complications identified.

Both Yu et al. (2018) and Wang et al. (2015) identified that the type of cancer entity present in their patients impacted the incidence of complications. Wang et al. (2015) considered this relationship in more depth, identifying why particular malignancies may have had an impact. These studies by Yu et al. (2018) and Wang et al. (2015) presented contrasting results regarding the significance of age as a risk factor, with Yu et al. (2018) finding that age was significant, and Wang et al. (2015) concluding the opposite. Whilst Yu et al. (2018) used multivariate analysis to determine this, Wang et al. (2015) found that in univariate analysis, age was a factor associated with higher infection rates, but in multivariate analysis, it was not. However, the smaller sample size in study by Yu et al. (2018) must be considered, as it may explain why they found age to be a significant risk factor. However, there is still uncertainty surrounding this.

7. Comparing PICCs and TIVAPs

Comparing the Risks and Complications of PICCs and TIVAPs

Taxbro et al. (2019) found that PICCs correlated with higher risks of complications compared to TIVAPs. The primary complication discussed was thrombosis, followed by catheter related adverse events (thrombotic events, occlusion, infections and mechanical issues). They also considered patient satisfaction.

Regarding risk factors that contributed to these complications, catheter type was the only statistically significant independent risk factor found. (Taxbro et al., 2019)

PICC related thrombotic events took place more frequently than for TIVAPs. When combining all complications into a composite variable, PICC patients experienced significantly higher incidences of complications. (Taxbro et al., 2019)

Regarding patient satisfaction, PICCs had a greater effect on daily activities compared to TIVAPs. (Taxbro et al., 2019) These findings were consistent with the retrospective study by Akhtar and Lee (2021).

Evaluation of the Studies

While Taxbro et al. (2019) and Akhtar and Lee (2021) concluded similar findings, there were key differences in their studies. Taxbro et al. (2019) conducted a randomised trial whereas Akhtar and Lee (2021) conducted a retrospective study. As mentioned above, retrospective studies lend themselves to more bias as they involve searching for specific patterns and trends in the data being analysed. Randomised trials, on

the other hand, are conducted in environments that can reduce selection bias. Taxbro et al. (2019) used a computer-generated randomisation sequence prepared by an independent statistician to stratify the selection of two blocks from 4 in their study. This is seemingly an effective randomisation method used in the trial, i.e. used to reduce bias.

In the study by Akhtar and Lee (2021), the results obtained were qualitative—they were unable to make a formal statistical comparison of the PICCs and TIVAPs. Additionally, given that it was a single-centre study, the representativeness of the results obtained is limited.

The trial by Taxbro et al. (2019) focused on patients with non-haematological cancer. Given the study conducted by Wang et al. (2015), it is unclear whether their findings would be consistent for hematological cancers too.

The trial by Taxbro et al. (2019) also included a wide range of different cancer entities receiving adjuvant and palliative care, which limits how applicable the results are to specific treatments and malignancies. For instance, Tang et al. (2019) recommended the use of PICCs for breast cancer patients in need of short term chemotherapy, and TIVAPs for long term chemotherapy.

However, in the study conducted by Qi et al. (2019), TIVAPs were identified as the ideal venous access device for patients with thyroid cancer.

Conclusion

In summary, the major complications associated with PICC use include phlebitis, thrombosis, infections and occlusion, along with mechanical problems. These were found to correlate with drinking, prior surgery history and immunotherapy. (Cao et al., 2020) (Mielke et al., 2020)

Whilst Cao et al. (2020) acquired data from a larger sample of patients regarding PICC usage in general, Mielke et al. (2020) concluded findings more specific to oncology patients. Lumen size was a factor associated with PICC related complications that was not considered by Cao et al. (2020).

For TIVAP use, the major complications identified included mechanical issues and infection, as well as occlusion. The risks associated with these include age, type of cancer entity, and adjuvant versus non-adjuvant chemotherapy. (Yu et al., 2018) (Wang et al., 2015) (Bassi et al., 2012)

Although Yu et al. (2018) and Wang et al. (2015) discovered similar information, their results did not align with regards to the impact of a patient's age on TIVAP related complications, raising questions on the overall significance of age.

Taxbro et al. (2019) and Akhtar and Lee (2021) both concluded that TIVAP usage correlated with lower risk of complications compared to PICCs for cancer patients.

Taxbro et al. (2019) conducted a randomised trial whereas Akhtar and Lee (2021) conducted a retrospective study. Akhtar and Lee (2021) performed a single-centre study, which limits how representative their results are. The results from the study by Taxbro et al. (2019) also may not be applicable to all types of cancers, and non-adjuvant treatments.

This review reveals potential future areas of research surrounding this topic, including a deeper examination of how age correlates with venous access device related complications for both devices, the incidence of complications for both of these devices in adjuvant settings, how suitable PICCs and TIVAPs are for different types of cancer and how vulnerable patients with specific types of cancer are to the complications that arise using these devices. Outside the scope of cancer treatments, an investigation into the risks and incidence of complications for these two devices for other treatments could be carried out. All of this could combine to introduce further research into how these devices can be improved in order to reduce their respective risks and complications overall.

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