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Is the use of a PORT as opposed to a PICC more effective in improving quality of life in patients receiving chemotherapy?

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ABSTRACT

Objective: The objective of this selective EBM review is to determine whether or not "Is the use of a PORT as opposed to a PICC more effective in improving quality of life in patients receiving chemotherapy?"

Study Design: Review of three randomized control trials (RCTs) including one monocentric RCT, one two-centre RCT, and one multi-centered RCT.

Data Sources: All articles were published in English and taken from peer-reviewed journals using PubMed. All articles were published between 2014-2020 and chosen based on their relevance to the clinical question.

Outcome Measured: The outcome measured was quality of life (QoL). The studies used patient-reported homemade questionnaires and/or a validated QLQ-C30 questionnaire. For consistency assessments provided at a 6-month interval from insertion were utilized.

Results: In the RCT led by Taxbro, et al.[1] indicated no significant difference in QoL overall, but a significant difference in QoL for certain activities encompassing global health. A significant difference was noted in taking a bath (p=0.004) and working out (p=0.052). No significant difference was noted with discomfort (p=0.616), showering (p=0.382), arm movement (p=1.000), or getting dressed (p=1.000). Patel, et al.[4] examined patient-rated questionnaires that were used to generally assess QoL. Although specific data was not provided, results stated: "no significant differences were noted between the groups in the quality-of-life measures examined." Patel et al. did note a significant difference in median dwell time for PORTs compared to PICCs (p=0.0057) which may have impacted results if it were included in the questionnaire.[4] In the RCT performed by Clatot, et al., the validated questionnaire used indicated patients with PORTs did not indicate improved QoL compared to patients receiving PICCs (p=0.48). The mean difference between PICCs and PORTs was 3.4 (p=0.48).[8] The study also contained a homemade questionnaire assessing global satisfaction as QoL. Results were reported as mean scores. Comparison of the PICC and PORT groups indicated no significant differences (p=0.78).

Conclusion: One of the studies demonstrated that patients with PICCs reported a significantly worse QoL. Two studies indicated QoL did not differ significantly between patients receiving chemotherapy via a PICC or a PORT.

Key Words: peripherally inserted central catheter, implanted port catheter, quality of life

INTRODUCTION

Chemotherapy is used to treat a wide range of cancers in both adults and children. While best practices for use and duration have been established according to cancer types, optimal practices for vascular access remain under debate.[1] Between 2018 and 2040, an estimated number of patients requiring first-line chemotherapy globally each year will increase 53% from 9.8 million to 15 million if all patients are treated according to evidence-based guidelines.[2] Consequently, understanding the safety and reliability of a venous access device is becoming increasingly important for both medical providers and patients.

With the expansion of cancer treatments in the United States, the economic burden of cancer has increased significantly.[3] The estimated prevalence cost of cancer in 2010 was $124.5 billion, and if incidence, survival, and costs of care remained at constant levels, the cost was projected to increase to 157.8 billion by the year 2020.[3] Estimates and projections are comprised of direct medical costs and indirect costs. It is difficult to determine an exact amount for each component, however, it is known treatments including chemotherapy are a substantial factor within direct medical costs.[3] Safe and reliable venous access devices (VADs) not only play an important role in controlling costs but also contribute to quality patient care.[3]

The use of central venous catheters (CVCs) has become a critical component of patient care during chemotherapy treatment. Catheters are used to provide prolonged access to the bloodstream for the effective delivery of chemotherapy and blood products.[4] Some benefits of using CVCs for chemotherapy treatment included reduced needle sticks, avoidance of bruising or bleeding, and administering more than one medication at a time.[5] The United States purchases approximately 150 million intravenous catheters per year.[5] Two types of widely used catheters are peripherally inserted central catheters (PICCs) and implanted central venous catheters

(PORTs). A PICC is commonly inserted in the basilic, brachial, or cephalic vein.[5] PICCs are more easily inserted than PORTs and are often used in patients requiring up to six months of intravenous chemotherapy. They require frequent flushing and dressing changes.[5] PORTs are surgically implanted in the chest wall or upper arm and require less frequent flushing but are more difficult and time-consuming to insert and remove.[6] PICCs and PORTs may influence quality of life (QoL) differently due to factors such as visibility, pain, clothing restrictions, and interference with activities of daily living; however, scientific evidence outlining patient satisfaction is limited. This paper evaluates three randomized controlled trials examining the effects of a PORT as opposed to a PICC venous access device on QoL in patients receiving chemotherapy.

OBJECTIVE

The objective of this systematic review is to determine whether "Is the use of a PORT as opposed to a PICC more effective in improving quality of life in patients receiving chemotherapy?"

METHODS

The population targeted for this review included male and female patients $\geq$ 18 years of age diagnosed with cancer and requiring chemotherapy. The intervention being examined for venous access is a PORT, the comparator is a PICC. The outcome being measured is improved quality of life. The types of studies included in this evidence-based medicine (EBM) review are an open-labeled, two-centre RCT, a multi-centered RCT, and a mono-centric, phase II RCT.

All articles were published in English in peer-reviewed journals between 2014-2020. The articles were obtained from PubMed and selected based on relevance to clinical questions as well as the content of patient-oriented evidence that matters (POEMS). Keywords used to acquire the

articles included “peripherally inserted central catheter”, “implanted central venous catheter”, “quality of life”, and “chemotherapy”. Inclusion criteria were articles published within the last 10 years, adults ≥ 18 years old, and randomized controlled trials. Exclusion criteria included studies >10 years old, pediatric patients, non-cancer patients, and systematic reviews. A summary of statistics reported includes p-values, NNTs, mean scores and subjective rating scales. Table 1 denotes the demographics and characteristics of the included studies.

Table 1 – Demographics and Characteristics of Included Studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interven-tions
Taxbro (2019)[1]	Open-Labeled Two-centre RCT	399	≥18 yrs	Life expectancy longer than 4 weeks, requiring chemotherapy through venous access	Ongoing severe systemic infection, clinically significant upper extremity/ central DVT, inability to communicate, severe coagulopathy, or an imminent need for dialysis fistula	15	PICC vs PORT
Patel (2014)[4]	Multi-centred RCT	70	≥18 yrs	Adult patients with non-hematological malignancy, chemotherapy through venous access, projected life expectancy ≥ 3 months	Patients with haematological cancer, children and adolescent patients	2	PICC vs PORT
Clatot (2020)[7]	Mono-centric phase II RCT	253	>18	Females, histologically confirmed EBC treated with curative intent and an indication of anthracycline + taxane-based ACT	Males, Metastatic breast cancer, altered haemostasis, inflammatory breast cancer, cutaneous disease, thrombosis of upper body in last 12 months, inclusion in trial, tracheotomy	3	PICC vs PORT

OUTCOMES MEASURED

The outcome measured in this EBM review included improved QoL for patients receiving chemotherapy through a PICC or PORT device. To more globally assess QoL, multiple outcomes were combined in all three studies. In the study conducted by Taxbro et al.,[1] QoL was measured using a numeric rating scale (NRS) completed by patients regarding interference with daily activities and discomfort. A generalized discomfort score was calculated by totaling individual component scores and p-values were obtained by use of the Chi^2 or Fishers test.[1] In the study by Patel et al.,[4] patients were asked to rate QoL by lifestyle factors in the following manner: *not at all*, *a little*, or *quite a bit* using a non-validated, study-specific central venous line questionnaire. Data was collected every three weeks during the study until catheter removal or six months, whichever was sooner.[4] In the study by Clatot et al.,[7] the European Organisation for Research and Treatment of Cancer QLQ-C30 score along with a home-made device satisfaction questionnaire dedicated to venous devices were used to analyze QoL.[7] The QLQ-C30 included functional and symptoms scales to globally assess health status. The analysis was given post-implantation, mid-treatment, and end of treatment. The satisfaction questionnaire forms comprised of designated questions to evaluate four scales: anxiety/pain, discomfort, satisfaction, and global acceptance. Questionnaires were self-administered four times throughout the study: the day of the first chemotherapy administration (after implantation), mid-treatment, three weeks after last administration (end of treatment), and 35 weeks after implantation (end of follow-up).[7] The overall rating used a 4-point scale, 1 indicating not at all and 4 indicating a lot.[7]

RESULTS

Taxbro et al. conducted an open-labeled, two-centre RCT that compared two types of central venous catheters (PICC and PORT) in patients with non-haematological cancer. A total

of 399 participants ≥18 years old, with life expectancy longer than 4 weeks, and requiring chemotherapy through a central venous device were selected for this study between March 2013 and February 2017.[1] Individuals were chosen based on specific inclusion and exclusion criteria detailed in Table 1. Patients were randomized in a 1:1 allocation ratio to either a PICC or a PORT at two county oncology centers in Sweden. In total, 201 patients received a PICC while 198 patients received a PORT.[1] The randomization sequence was computer-generated and prepared by an independent statistician using a block size of four and stratification to the two centers.[1] Due to the properties of the catheters, it was not feasible to "blind" the patient, clinician, or trial assessors. Statistical data used to measure generalized discomfort in this study, presented as p-values, was collected from both groups after catheter implantation and at follow-up intervals of 1, 3, 6, and 12 months. To keep consistency between study results, this review will focus on a six-month follow-up interval.

For this EMB review, patient-reported multiple outcomes were combined to more globally assess QoL. Results were 54.2% in the PICC group and 28.2% in the PORT group (Table 2).[1] The PICC group results showed statistical significance in interference with some daily activities including bathing ($p= 0.004$) and working out ($p= 0.052$). No significant difference was reported with arm movement, showering, and getting dressed.[1] The study also reported a p-value of 0.616 for discomfort indicating no statistical significance amongst the groups. The calculated NNT, -3, demonstrated a small treatment effect and implies no clinical significance (Table 3).[1]

Table 2. Comparison of Discomfort and Interference of the Study Groups Month 6 After Insertion (data from Taxbro et al.)[1]

	Patient Reported (%)		p-value
	PICC	PORT	
Discomfort	5/39 (12.8)	19/105 (18.1)	0.616
Interference: Showering	3/40 (7.5)	4/107 (3.6)	0.382
Taking a bath	4/17 (23.5)	2/98 (2)	0.004
Working out	3/38 (7.9)	1/110 (0.9)	0.052
Moving Arm	1/40 (2.5)	2/110 (1.8)	1.000
Getting Dressed	0/40 (0)	2/110 (1.8)	1.000

Table 3. Calculations for Treatment from Taxbro et al.[1]

Study	CER	EER	RBI	ABI	NNT
Taxbro et al.	0.54	0.28	0.48	0.38	-3

Patel et al. conducted a multi-centered RCT similar in design to Taxbro et al. examining the self-reported quality of life variables between PICCs and PORTS in the delivery of chemotherapy in patients with non-haematological cancer. Seventy patients from three Australian centers: Flinders Medical Centre (n=45), The Queen Elizabeth Hospital (n=2), and Monash Cancer Centre (n=23) were randomized 1:1 to receive a PICC or a PORT device. Eighty-one patients were deemed eligible between December 2004 and January 2010, however, 11 declined participation due to a preference of CVC type. The 70 remaining patients (29-84 years of age) with a projected life expectancy of at least 3 months and requiring chemotherapy through a central venous device were randomized, but 2 withdrew prior to device insertion.[4] Inclusion and exclusion criteria are noted in Table 1.

All three facilities in this study specified the PICC line tip was placed at the caval-atrial junction, and the position was checked radiologically at the end of the procedure.[4] PORT insertion was performed by a surgeon on all patients. Catheter care for both types of devices was performed by a specialist trained catheter care nursing team in the hospitals.[4] Notably, the median dwell time was longer for PORTs compared to PICCs.[4] The calculated p-values for

median dwell time was 0.0057 indicating a statistical significance in both amongst patients in this study. See values presented in Table 4 below.

Quality of life data was obtained from 36 patients (53%) using a non-validated study-specific questionnaire covering functional status, sleep, and hygiene disturbance. Data was collected in three-week intervals until catheter removal with a maximum of six months.[4] Numerical figures on quality of life were not provided by researchers; therefore, a NNT could not be calculated. Subjective measures summarizing patient questionnaire responses indicated the PICC group reported "not at all" to "a little" interference with lifestyle factors in five of the seven areas examined: *clothing, help required. for CVC problems, sleep, activities of daily living,* and *social life.* "A little" to "quite a bit" interference was noted in *personal hygiene* and *work activities*.[4] The PORT intervention group demonstrated no area rated greater than "a little" interference with all seven lifestyle factors.[4] There was no reported p-value, however, the author did report that "No significant differences were noted between the groups in the quality-of-life measures examined."[4]

Table 4. Comparison of Dwell Time Between Groups (data from Patel et al.[4])

	PICC Group	PORT Group	p-value
Median dwell time (days)	115	160	P=0.0057

The final study conducted by Clatot et al.[7] was a monocentric, phase II, RCT evaluating QoL variables between PICCs and PORTS in the delivery of adjuvant chemotherapy (ACT) in patients with early breast cancer (EBC). Between February 2014 and May 2018, 751 patients from the Henri Becquerel Cancer Centre in France were screened for the study. From that population, 189 patients were deemed ineligible and 306 refused to participate. The remaining 256 patients were randomized by a computer at a 1:1 allocation ratio to receive a PICC (n=128) or a PORT (n=128) device.[7] Three patients withdrew consent after randomization and were

excluded from the final analysis. Inclusion and exclusion criteria for the participating 253 patients (30-74 years of age) are noted in Table 1.

PICC devices were implanted using the basilic or brachial vein and PORTs were implanted using the jugular or subclavian vein. PICCs were removed on the day of the last chemotherapy administration. PORTs were removed 4 weeks after the last chemotherapy administration. Patients in this study by Clatot et al.[7] provided ratings on the day of the first chemotherapy administration (post-implantation), at mid-course of chemotherapy treatment (mid-treatment), at 3 weeks after last chemotherapy administration (end of treatment), and at 35 weeks after implantation (end of follow-up). Due to the low response rate, only the results of the first 3 times were detailed using the EORTC QLQ-C30 analysis.[7] For consistency with time comparisons among the studies, this review will focus on end of treatment data.

The statistical data used by Clatot et al. to measure QoL by each group was presented as mean values, standard deviation, and p-values.[7] Data was obtained from a validated questionnaire, The European Organization for Research and Treatment of Cancer's cancer-specific quality of life questionnaire (EORTC QLQ-C30). The questionnaire consists of functional and symptom scales in addition to a global health status/quality of life (GHS/QoL). Due to clinical relevance to this review's question, only the GHS/QoL data is being utilized. The PICC comparator group showed a mean score of 64.4 with a standard deviation of 18.9 at post-implantation.[7] The p-value for scores was 0.48, demonstrating no significant difference in QoL as shown in Table 5.[7]

Table 5. EORTC QLQ-C30 Global Health Status Analysis Between PICC and PORT Groups (data from Clatot et al.[7])

	Mean ± SD	Mean Difference Between Groups (calculated)	P-Value
PICC Group	64.4 ± 18.9		
PORT Group (Intervention)	61 ± 21.4	3.4	0.48

The second type of data used by Clatot et al. to measure QoL was a self-administered, homemade patient questionnaire.[7] Results were presented as mean values and p-values. The PICC group showed a mean global score of 93.3 end treatment.[7] The PORT intervention group demonstrated a mean global score of 93.5 end treatment.[7] The p-value for global scores was p=0.78 end treatment indicating the results were not statistically significant within the population.[7] The values for this study can be seen in Table 6 below.

TABLE 6. Catheter-Related Global Satisfaction End Treatment (data from Clatot et al.[7])

	Mean	P-Value
PICC Group	93.3	P=0.78
PORT Group Intervention	93.5	

DISCUSSION

Over the last decade, new chemotherapy combinations and more complex treatment regimens have been developed to care for cancer patients.[5] As a result, vascular access devices are being widely used to facilitate these treatments. Although VADs play an important role in patient care, there is a lack of conclusive data in the literature supporting the choice of the most appropriate device, particularly in terms of quality of life. The objective of this systematic review was to determine if the use of a PORT as opposed to a PICC is more effective in improving QoL in patients receiving chemotherapy. The three articles reviewed in this EBM demonstrated a small treatment effect and indicated no significant overall improvement in QoL between patients receiving a PICC or a PORT. Taxbro et al.[1], who had the largest sample population of the three studies, demonstrated an insignificant overall difference in QoL amongst the groups; however, PORTS were perceived to have less effect on specific daily activities contributing to the overall score. Significant differences were reported for taking a bath (p-value = 0.004) and working out (p-value = 0.052).[4]

The study conducted by Patel et al.[4] which had the smallest sample population out of the three studies, demonstrated patients who received a PICC reported a greater impact in *hygiene and work activities* than patients with a PORT. Patients with a PORT rated less overall interference with lifestyle factors. Although statistical data was not provided, the study's authors reported no significant differences were noted between the groups.[4] Interestingly, Patel et al. did suggest a need for additional studies to further examine the statistical significance in the median dwell time between PICCs and PORTs and its possible effect on QoL.[4] Clatot et al. performed a study generalizable to only one center using two types of questionnaires (one validated and one homemade) to assess global health status as QoL. Results of the validated questionnaire yielded a mean score difference of 3.4 and a p-value of 0.48 indicating no significant difference in QoL between PICCs and PORTs.[7] The homemade questionnaire yielded a group comparison p-value of 0.78 also indicating no significant difference between PICC and PORT groups.[7]

The studies used in this review consisted of several limitations. In all three studies, participants were unable to be kept "blind" to the intervention.[1,4,8] This could present a potential impact or bias due to patient and physician device preference. The three studies also contained small sample sizes. Patel et al. related slow patient recruitment and failure to reach target sample size to patient and physician preference, refusal, and death.[4] Taxbro et al. and Clatot et al. reported a high participant refusal rate of 54% and 51% respectively.[4,7] Lastly, all three studies mentioned the need for a validated or refined questionnaire focusing solely on QoL factors. The studies performed by Taxbro et al. and Patel et al. used non-validated, homemade questionnaires. The study by Clatot used one validated and one non-validated questionnaire; however, both measures indicated no significant difference in QoL.[7]

Additional limitations were present within the individual studies. The studies by Taxbro et al.,[1] and Clatot et al.[7] noted a difference in "passive" dwell and exposure time for patients with PORTs, which could influence the interpretation of time-dependent data. Patients in Taxbro et al.[1]'s study had a wide range of solid tumor cancers and could be receiving adjuvant or palliative care. This can limit the ability to interpret results regarding specific diagnoses.[1] Patel et al. indicated possible compromise due to local-regional factors such as availability of skills and resources.[4] Expertise at local hospitals and cancer centers with insertion and management of a VAD may vary. Patel et al.'s study contained three centers; therefore, a higher level of variability may have occurred. Clatot et al.[7] identified a difference in implantation sites for PICCs and PORTs as a limitation. Heterogeneity of catheter positioning among patients may have increased validity in the results of the study.

CONCLUSION

All three randomized controlled trials in this EBM review yielded a lack of evidence to demonstrate improved quality of life for oncology patients using a PORT compared to a PICC while receiving chemotherapy. Studies completed by Taxbro et al. and Clatot et al. found a small treatment effect as p-values and NNT did not demonstrate a statistical significance. P-values were not given in the Patel et al. study; however, the authors noted "no statistical difference between groups" therefore, it can be extrapolated that the treatment effect was small.

Future studies evaluating and comparing this aspect of care are needed to assess quality of life more adequately. Additional trials are needed with a larger sample size given the indicated refusal rate of participants. Additionally, considering differences in cultural and regional factors including availability of skills and resources for inserting and managing central venous catheters and median exposure time between devices would be of greater benefit.[4] Questionnaire

refinement and validation in further studies are also essential as patient comments identified interferences with QoL that were not included on the questionnaire but were important to patient lifestyle.[4] At the time of my research, additional information on current ongoing studies was not found; however, these devices continue to be used regularly to gain venous access.[6] Reliable data on this essential aspect of care is vital in the quest to provide improved QoL for the millions of patients receiving chemotherapy treatments each year.

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