

Evaluation of Correlations between Underlying Disease and Port Complications

Evaluation von Zusammenhängen zwischen Grunderkrankung und Portkomplikationen

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Abstract



Purpose: Evaluation of correlations between underlying disease and port complications.

Materials and Methods: Retrospective analysis of a data set of 3160 port systems, which had been interventionally implanted over a period of 10 years. Of these, 1393 were included in the final evaluation. The 7 most common underlying diseases and port-induced complications were considered. Port-related thrombotic events, port pocket infections as well as the port-induced sepsis were evaluated and classified as either early or late complications.

Results: In 1393 ports, 131 experienced complications. Of these, 22.1% (n=29) were early and 79.6% (n=102) late complications. The overall incidence rate of late complications was 0.253/1000 observed days. It differed significantly between the underlying diseases ($p < 0.001$) and was significantly lower in colon carcinoma when compared with pancreatic ($p = 0.049$), gastric ($p = 0.012$) and bronchial carcinoma ($p = 0.042$). The incidence rate of the port sepsis between the underlying diseases also differed significantly ($p = 0.006$) and had the highest rate in gastric and bronchial carcinoma. The occurrence of a thrombotic event also showed a significant difference in the incidence rates between the underlying diseases ($p = 0.045$) and was highest in pancreatic and gastric carcinoma.

Conclusion: There are significant differences in the incidences of complications between the underlying diseases. Knowledge about this can help to improve the port-care and to take specific preventive measures.

Key Points:

- ▶ significant differences in the incidences of port complications between underlying diseases

- ▶ incidence rate of late complications significantly lower in colon carcinoma compared to pancreatic, gastric and bronchial carcinoma
- ▶ highest incidence rate of port sepsis in gastric and bronchial carcinoma
- ▶ highest incidence rate of thrombotic events in pancreatic and gastric carcinoma
- ▶ studies on specific prophylactic measures required

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Zusammenfassung



Ziel: Evaluation von Zusammenhängen zwischen Grunderkrankung und Portkomplikationen.

Material und Methode: Retrospektive Auswertung aus einem Gesamtdatensatz von 3160 Portsystemen, welche über einen Zeitraum von 10 Jahren interventionsradiologisch implantiert worden waren. Von diesen gingen 1393 in die endgültige Auswertung ein. Die 7 häufigsten Grunderkrankungen und portinduzierte Komplikationen wurden gegenübergestellt. Betrachtet wurden dabei portbedingte thrombotische Ereignisse, Porttascheninfektionen und die portinduzierte Sepsis, wobei Früh- und Spät komplikationen unterschieden wurden.

Ergebnisse: Bei 1393 Ports traten 131 Komplikationen auf. Hiervon waren 22,1% (n=29) Früh- und 79,6% (n=102) Spät komplikationen. Die Gesamtinzidenzrate der Spät komplikationen betrug 0,253/1000 Beobachtungstage. Sie unterschied sich signifikant zwischen den einzelnen Grunderkrankungen ($p < 0,001$) und zeigte beim Kolonkarzinomen eine signifikant niedrigere Inzidenzrate gegenüber dem Pankreas- ($p = 0,049$),

dem Magen- ($p=0,012$) und dem Bronchialkarzinom ($p=0,042$). Die Inzidenzrate der Portsepsis zwischen den Grunderkrankungen unterschied sich ebenfalls signifikant ($p=0,006$) und war beim Magen- sowie Bronchialkarzinom am größten. Für das Auftreten eines thrombotischen Ereignisses zeigte sich ebenfalls ein signifikanter Unterschied der Inzidenzraten zwischen den einzelnen Grunderkrankungen ($p=0,045$) und war dabei beim Pankreas- sowie Magenkarzinom am größten.

Schlussfolgerung: Es bestehen signifikante Unterschiede der Inzidenzen von Komplikationen zwischen den einzelnen Grunderkrankungen. Das Wissen hierüber kann helfen, die Portpflege zu verbessern und ggf. gezielte, präventive Maßnahmen zu ergreifen.

Introduction

Over the past few decades, port systems have been used as indwelling venous catheter systems. Their area of application is very broad, ranging from therapeutic applications for chemotherapy, parenteral nutrition, administration of antibiotics, fluid replacement to diagnostic purposes such as taking blood samples and administering contrast agent for medical imaging [1–5]. Of these examples, administering chemotherapy drugs is by far the most common indication for implanting a port system.

The different implantation techniques are commonly known and established, while the associated advantages and risks have been extensively discussed and described. Numerous articles have focused on the complication rates associated with the implantation [6–9], and the therapy options for port complications have already been repeatedly examined [10–12].

It is also known that the various chemotherapy regimens used in treating the particular underlying diseases entail side effects of varying degrees. A common, undesired effect is a compromised immune system, which increases the risk of infection. One of the most serious complications posed by an implanted port system is the appearance of port-induced sepsis [13, 14].

It is also known that an advanced degree of metastasis or malignant tumor with a high one-year mortality rate (e.g. pancreatic cancer) entails elevated thrombophilia [15, 16], which can in turn increase the risk of catheter lumen occlusion.

This retrospective study aims to evaluate correlations between underlying disease and port complications. The results should contribute to formulating disease-specific management for the use and care of port systems for the purpose of minimizing complications and ensuring the longest possible usability of the system.

Material and methods

Data was collected in a monocentric, retrospective study covering a period of 10 years (January 1, 2000 through December 31, 2009).

Our interventional radiology division implanted a total of 3160 ports in ten years. The preferred implantation technique was using ultrasound-guided access via the right internal jugular vein and infraclavicular implantation of the

port capsule followed by anchoring to the pectoral fascia. To ensure a follow-up observation period of at least one year, data collection was scheduled to end on December 31, 2009.

Over 100 different referral diagnoses (ICD-10) were recorded. To obtain meaningful group parameters for statistical processing, only the 7 most common clinical pictures were observed.

Port-related thrombotic events and infections were evaluated, the latter being further subdivided into port pocket infections and port-induced sepsis.

Definitions

Per the recommendations Society of Interventional Radiology (SIR), complications were divided into early complications (24 h to 30 d post op) and late complications (> 30 d post op) depending on when they appeared.

Catheter-associated thrombotic events can appear as a) mural thrombi at the catheter tip, b) thrombi occluding the catheter lumen and c) fibrin coatings.

Port pocket infections manifest themselves as local erythema with overheating and tenderness upon palpation that can involve the formation of pus during a later stage.

Port system-induced sepsis is defined by SIR as an infection of unknown focus, the symptoms of which subside within 48 hours of port explantation [17].

Only port systems that had reached an end point were included in the evaluation. End points included the appearance of complications, port explantation, patient death during the observation period as well as reaching the follow-up observation time with an implanted port system. Upon reaching an endpoint, the port system was not subjected to further observation.

The catheter observation period was the interval of time between port implantation and the respective endpoint.

Port imaging in cases of port dysfunction

All patients referred with “port dysfunction” were examined by our interventional radiologists in the angi suite.

Prior to the examination, all patients were provided with oral and written information.

Following sterile preparation, patients were fitted with a port needle or any port needle present on the port system was used. Antegrade and retrograde testing of the port system was performed by injecting 10 ml of NaCl.

If mildly elevated infusion pressure was all it took to break up the thrombotic formation, then the intervention was deemed as successfully completed following a final flushing.

If the dysfunction was not remedied, then 5 to 10 ml of contrast agent were injected via the port system (hence “port imaging”). Using digital subtraction angiography (DSA), the superior vena cava was tested for patency and normal flow of contrast agent. The system was finally flushed with 1000 I.U. of heparin. If no patency was established, then lysis was attempted by subsequently performing another round of port imaging. If this proved unsuccessful, then the system was explanted.

Data analysis and statistical methods

Data was collected via the radiological information system (RIS) Robsys, the Orbis database (Orbis Open Med, AGFA AG, Bonn) as well as the hospital-wide SAP database (SAP for Healthcare, SAP AG, Walldorf).

Date of birth, sex, underlying disease, implantation indication, implantation modalities and the point in time of port complications were ascertained.

The Poisson-Regression model was employed to examine the influence of the underlying disease on the incidences of each examined complication. If the underlying disease was found to have a significant influence on incidence, a post-hoc pairwise comparison of the underlying diseases was undertaken using a Bonferroni-Holm correction. Data analysis was performed using the software SPSS Statistics 21.9 (IBM, USA). Significance was set at 0.05.

Results

A total of 1393 port systems were evaluated, the seven most common underlying diseases being presented in **Table 1**. Total observation period was 403.019 days. In total 131 (9.4%) complications appeared. **Fig. 1** presents the respective frequencies of the appearing complications, divided into early and late events.

The incidence rates of early complications among the individual underlying disease vary significantly ($p=0.019$). In relation to underlying disease, early complications showed the following distribution: Breast carcinoma (7/121, 5.8%), ovarian carcinoma (5/116, 4.3%), colorectal carcinoma (7/172, 4.0%), bronchial carcinoma (6/226, 2.7%) and pan-

creatic carcinoma (4/427, 0.9%). However, pairwise comparison of the underlying diseases showed no significantly higher incidence rate for any of the underlying diseases. No early complications were recorded for gastric carcinoma or non-Hodgkin's lymphoma.

The incidence rate of the appearing late complications (overall 0.253/1000 days of observation) varied significantly among the individual underlying diseases ($p < 0.001$), with a significantly lower incidence rate being observed in colorectal carcinoma compared to pancreatic ($p=0.049$), bronchial ($p=0.042$) and gastric carcinoma ($p=0.012$), **Table 2**. The incidence rate for port sepsis varied significantly ($p=0.006$) among the observed underlying diseases, being greatest for gastric carcinoma (0.285/1000 days of observation) and bronchial carcinoma (0.260/1000 days of observation). With regard to the appearance of thrombotic events, there was likewise significant difference among the individual underlying diseases ($p=0.045$), with pancreatic carcinoma (0.216/1000 days of observation) and gastric carcinoma (0.175/1000 days of observation) having the highest incidence rates.

Discussion

As the results of this and other studies demonstrate, port-associated thrombotic events represent one of the most common type of port complications [18–20]. When it comes to underlying disease, our study found pancreatic carcinoma to have the highest rate of incidence port-associated thrombotic events, which is consistent with the findings of Chew et al. [21]. To our knowledge, there are no studies to date that have examined thrombosis in and at

underlying disease	n	%	days of observation	average	median
pancreatic carcinoma	427	30.7	86.737	203	169
bronchial carcinoma	226	16.2	35.702	158	121
gastric carcinoma	211	15.1	57.886	274	216
colorectal carcinoma	172	12.3	88.590	515	538
breast carcinoma	121	8.7	27.020	223	115
non-Hodgkin lymphoma	120	8.6	54.080	451	379
ovarian carcinoma	116	8.3	53.004	457	402
total	1393	100	403.019	289	191

Table 1 Observation times of port systems in relation to the underlying disease.

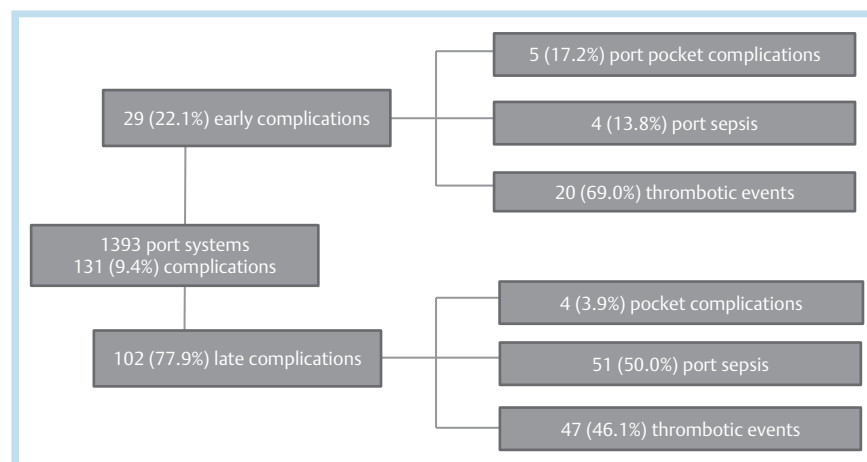


Fig. 1 Flow chart showing total complications divided into early and late complications.

Table 2 Late complications in relation to the underlying disease.

underlying disease	port pocket infection				thrombotic events			port-associated sepsis			total		
	n	n	%	/1000 days of observation	n	%	/1000 days of observation	n	%	/1000 days of observation	n	%	/1000 days of observation
pancreatic carcinoma	423	2	0.5	0.025	18	4.4	0.216	11	2.7	0.134	31	7.3	0.358
bronchial carcinoma	220	1	0.5	0.031	5	2.4	0.149	9	4.2	0.260	15	6.8	0.422
gastric carcinoma	211	0	0.0	0.000	9	4.6	0.175	16	7.9	0.285	25	11.8	0.432
colorectal carcinoma	165	0	0.0	0.000	4	2.5	0.046	7	4.3	0.080	11	6.7	0.124
breast carcinoma	114	1	0.9	0.038	2	1.8	0.075	2	1.8	0.075	5	4.4	0.186
non-Hodgkin's lymphoma	120	0	0.0	0.000	2	1.7	0.038	5	4.2	0.095	7	5.8	0.129
ovarian carcinoma	111	0	0.0	0.000	7	6.4	0.134	1	1.0	0.020	8	7.2	0.151

the port system in relation to underlying disease. The state of research on venous thromboembolic events in relation to malignant underlying diseases is significantly better. It is known that tumor cells influence coagulation and angiogenesis through different mechanisms [22]. In addition, an increased rate of embolism has been described when aggressive tumors and an increasing degree of metastasis are present [15, 21]. The rate of embolism is additionally influenced by co-morbidities, surgical interventions and chemotherapy regimen [23]. Thromboembolic events also occur most frequently in the first month following diagnosis [23], which may be attributed to therapy beginning with surgical intervention and initial chemotherapy.

Thoroughly flushing the system prior to use is a well-known measure for preventing port-associated thrombosis [24]. If a thrombotic formation has already appeared, lysis or fibrin-stripping are very promising methods [10]. Unless contraindicated, early systemic prophylaxis with low-molecular heparin has been discussed for preventing deep vein thrombosis in cases involving biologically aggressive tumors or metastasis [25–28]. This method may also have another positive effect by possibly reducing fibrin coatings and thrombi from the catheter tip. Subsequent studies with concomitant systemic thromboembolism prophylaxis would be required to examine to what extent this hypothesis is true.

The results of our study show that an increased number of port-related sepsis has been observed particularly for gastric carcinoma. This may possibly be due to the frequently early start of parenteral nutrition via the port system and the thereby increasing risk of port-related sepsis when insufficient port system care is practiced [29]. In addition, gastric carcinoma entails a higher incidence of thrombotic events. It has been suggested that thrombotic formations on the catheter can also pose an elevated risk of catheter-related sepsis [30, 31]. Our study is not in the position to address this statement, since port systems were observed only until the first appearing complication. In a pediatric study involving children with hematological diseases, taurolidine citrate was able to bring about a significant reduction in catheter-related sepsis [32]. A systematic survey study likewise demonstrated the advantage of heparin- or antibiotic-coated catheters over non-coated catheters [33]. Independent risk factors for a port-related sepsis include, among

other factors, cancer of the digestive system, cumulative number of days of catheter use and parenteral nutrition [29].

The weaknesses of our study could be that the tumor stage, the exact chemotherapy protocol, whether antithrombotic or antibiotic prophylaxis was performed and the number of times ports were used were not known. Furthermore, it cannot be ensured that all port complications were detected and recorded in the study, since treatment outside of our hospital cannot be excluded.

Summary

There are significant differences among the incidence rates of complications for individual underlying diseases. Knowing this can aid in performing systematic treatment and preventative measures, such as thromboembolism prophylaxis, to thereby prevent premature port dysfunction and possibly explantation as well. Additional studies on the effectiveness of these measures are required, however.

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