ILEIAC STENT PATENCY IN ONCOLOGIC PATIENTS WITH PERIPHERAL ARTERY DISEASE TREATED BY FEMORAL ENDARTERECTOMY AND ILIAC STENTING

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ABSTRACT

Introduction. Patients with peripheral artery disease and oncological comorbidities often face severe forms of the disease, with an increased risk of amputation and perioperative mortality. Femoral endarterectomy followed by iliac stenting is an alternative to aorto-femoral bypass with reduced perioperative risks. Despite successful revascularization, oncologic patients experience lower patency rates.

The objective of the study was to identify the factors responsible for lower iliac stent patency rates in oncologic patients.

Material and methods. We investigated 74 patients with severe iliac artery lesions and complete occlusion of the common femoral artery, who were divided into two groups: 25 patients with associated oncologic pathology and 49 non-oncologic patients. Subsequently, two subgroups were created for each group, to evaluate the impact of heart failure with impaired ejection fraction on stent patency. All patients underwent common

Resumé

Perméabilité des stents iliaques chez les patients oncologiques atteints de maladie artérielle périphérique traités par endartériectomie fémorale et pose de stent iliaque

Introduction. Les patients atteints de maladie artérielle périphérique et de comorbidités oncologiques sont souvent confrontés à des formes sévères de la maladie, avec un risque accru d’amputation et de mortalité périopératoire. L’endartériectomie fémorale suivie d’un stenting iliaque est une alternative au pontage aorto-fémoral avec des risques périopératoires réduits. Malgré une revascularisation réussie, les patients oncologiques connaissent des taux de perméabilité inférieurs.

L’objectif de l’étude était d’identifier les facteurs responsables de la baisse des taux de perméabilité des stents iliaques chez les patients oncologiques.
femoral artery endarterectomy followed by iliac stenting. The patency of iliac stents after one-year was assessed by Doppler ultrasound, and statistical analysis was performed using Kaplan-Meier survival curves.

**Results.** Oncologic patients had a lower one-year iliac stent patency rate (66.48%) compared to the control group (85.66%). Additionally, patients with impaired left ventricular ejection fraction (< 40%) were more prone to experiencing iliac stent occlusion after one year, particularly in the oncologic group (53.43% patency). Moreover, the oncologic group also exhibited a notably higher incidence of postoperative thrombosis.

**Conclusions.** Our study highlights a greater occurrence of postoperative thrombotic complications in oncologic patients. Moreover, heart failure with reduced ejection fraction could be a potential contributor to early stent occlusion.

**Keywords:** hybrid vascular surgery, oncologic patients, peripheral artery disease, mid-term patency, amputation-free survival.

**List of abbreviations**
- AFS – amputation free survival
- CFA – common femoral artery
- CI – confidence interval
- EF – ejection fraction
- OS – overall survival
- PAD – peripheral artery disease

**Introduction**

Oncologic pathology is a significant global problem, with a continuously increasing incidence that affects millions of people. It is the second most common cause of mortality in the world, after cardiovascular diseases. In Europe alone, almost 4 million new cancer cases were diagnosed in 2018, with nearly 2 million associated deaths. Cancer patients are a vulnerable group who are frequently referred to a vascular surgery unit for advanced stages of peripheral arterial disease (PAD). Many of these patients have other severe cardiovascular morbidities, and up to 16% of them have diabetes, which raises the perioperative surgical risk. Due to the rapid progression of cancers, they are given treatment priority, and delayed oncologic treatment may lead to increased mortality rates. As a result, patients with associated PAD may end up with severe forms of the disease, with an increased risk of amputation and elevated perioperative mortality. However, minimally invasive revascularization options reduce the incidence of major complications and offer viable solutions for frail patients. The endovascular approach is the ideal solution for all patients with high operative risk, but it is limited by the presence of long, calcified, occlusive plaques, especially for multifocal lesions associated with complete common femoral artery (CFA) occlusion (an important access route in endovascular revascularization). In patients for whom a strictly endovascular approach is insufficient, or whom present advanced multilevel arterial lesions, hybrid revascularization techniques (a combination of conventional surgery and endovascular techniques) can be used as a minimally invasive alternative to classic surgery. Femoral endarterectomy followed by iliac stenting is an alternative to aorto-femoral bypass, with similar results while minimizing perioperative risk. Even

Matériel et méthodes. Nous avons étudié 74 patients présentant des lésions sévères de l’artère iliaque et une occlusion complète de l’artère fémorale commune, qui ont été divisés en deux groupes : 25 patients avec une pathologie oncologique associée et 49 patients non oncologiques. Par la suite, deux sous-groupes ont été créés pour chaque groupe, afin d’évaluer l’impact de l’insuffisance cardiaque avec fraction d’éjection altérée sur la perméabilité du stent. Tous les patients ont eu une endartériectomie de l’artère fémorale commune suivie d’une pose de stent iliaque. La perméabilité des stents iliaques après un an a été évaluée par échographie Doppler et une analyse statistique a été réalisée à l’aide des courbes de survie de Kaplan-Meier.

**Résultats.** Les patients oncologiques avaient un taux de perméabilité du stent iliaque à un an inférieur (66,48 %) par rapport au groupe témoin (85,66 %). De plus, les patients avec une fraction d’éjection ventriculaire gauche altérée (< 40 %) étaient plus susceptibles de subir une occlusion de stent iliaque après un an, en particulier dans le groupe oncologique (53,43 % de perméabilité). De plus, le groupe oncologique présentait également une incidence nettement plus élevée de thrombose postopératoire.

**Conclusions.** Notre étude met en évidence une plus grande survenue de complications thrombotiques postopératoires chez les patients oncologiques. De plus, l’insuffisance cardiaque avec une fraction d’éjection réduite pourrait être un contributeur potentiel à l’occlusion précoce du stent.

**Mots-clés:** chirurgie vasculaire hybride, patients oncologiques, maladie artérielle périphérique, perméabilité à moyen terme, survie sans amputation.
though revascularization can be achieved for most patients with multi-level lesions, lower patency rates were observed in oncologic patients.

**The Objective of the Study** was to investigate the efficacy of femoral endarterectomy followed by iliac stenting for patients with severe iliac artery stenosis and complete CFA occlusion for oncologic patients (TransAtlantic Inter-Society Consensus - TASC D lesions). We also aimed to identify the factors responsible for lower patency rates in cancer patients and provide preliminary mid-term results regarding ilio-femoral revascularization of the aforementioned group.

**Materials and Methods**

We conducted a retrospective observational study in St. Pantelimon Emergency Clinical Hospital, Bucharest, Romania, between January 2019 and December 2021. We included 74 patients with PAD with complete CFA occlusion and over 70% stenosis of the ipsilateral iliac artery that required revascularization. The patients were divided into two groups: 25 consecutive patients with associated oncologic pathology and 49 consecutive non-oncologic patients. The age distribution was similar in both groups, and we were able to perform statistical comparisons. Two additional subgroups were created for each group, to separate the patients with moderately to severely impaired ejection fraction (EF < 40%) of the left ventricle from the rest. Preoperatively, left ventricular function was assessed by echocardiography and PAD diagnosis was confirmed by computed tomography angiography (CTA). All patients underwent CFA endarterectomy followed by iliac stenting with bare metal stents, during the same procedure (hybrid revascularization), under general anesthesia. The oncologic group consisted of patients with malignant tumours, leukemias, and lymphomas, all of whom had a life expectancy of at least 2 years. We did not include minors in this study. The anticoagulant and antiplatelet treatment regimen followed was identical for the two groups.

We investigated the reason for admission, risk factors, associated morbidities, intra-operative and post-operative complications for both groups. We evaluated mid-term (one year) patency, amputation-free survival (AFS), and overall survival (OS) as primary endpoints for both groups. We assessed mid-term iliac stent patency using Doppler ultrasound control, focusing only on primary patency, which is the amount of time that the stents were functional without requiring surgical or endovascular maintenance (assisted primary patency) or an additional intervention to compensate the arterial inflow or outflow (secondary patency). We considered primary patency as an expression of the longevity of the hybrid procedure, while reinterventions were analyzed separately as purely surgical or endovascular.

We used the Kaplan-Meier survival function for patency rates, AFS, and OS rates. We compared patient groups using the student t test and Fisher test, with a threshold of p < 0.05 for statistical significance.

| Table 1. General data, risk factors and comorbidities for oncologic and non-oncologic patients |
|-----------------------------------------------|-------------------------------|-----------------|----------------|----------------|
| Variable                                      | n (%)                         | Onc (25)        | Non-onco (49)  | p              |
| General                                       |                               |                 |                |                |
| Sex, M                                        | 19 (76)                       | 33 (67)         | 0.44           |                |
| Sex, F                                        | 6 (24)                        | 16 (33)         | 0.44           |                |
| Reason of admission                           |                               |                 |                |                |
| Disabling claudication                        | 10 (40)                       | 25 (51)         | 0.36           |                |
| Chronic limb threatening ischemia             | 15 (60)                       | 24 (49)         | 0.36           |                |
| Risk factors                                  |                               |                 |                |                |
| Smoking                                       | 20 (80)                       | 37 (76)         | 0.66           |                |
| Diabetes                                      | 9 (36)                        | 18 (37)         | 0.95           |                |
| Dyslipidemia                                  | 19 (76)                       | 40 (82)         | 0.56           |                |
| Comorbidities                                 |                               |                 |                |                |
| Hypertension                                  | 21 (84)                       | 37 (76)         | 0.40           |                |
| Chronic kidney disease (GFR < 30 ml/min/1.73m²)| 2 (8)                         | 0 (0.00)        | 0.04           |                |
| Coronary artery disease                       | 11 (44)                       | 12 (24)         | 0.08           |                |
| Cerebrovascular disease                       | 6 (24)                        | 14 (29)         | 0.67           |                |
| Heart failure (ejection fraction < 40%)       | 14 (56)                       | 14 (29)         | 0.02           |                |
| Chronic obstructive pulmonary disease         | 5 (20)                        | 7 (14)          | 0.52           |                |
This study was approved by the research ethics committee of St. Pantelimon Emergency Clinical Hospital, Bucharest, Romania (approval no 29/16.08.2022).

**RESULTS**

The study included 74 patients who had complete CFA occlusion and severe iliac stenosis (>70%). The oncologic group of 25 patients had a mean age of 72.28±9.96 years and the control group, comprised of 49 patients, had a mean age of 68.91±11.08 years. We compared their general data, risk factors and associated morbidities (Table 1), and found that most patients were males in both groups (p < 0.01). While a higher percentage of oncologic patients were admitted with severe forms of PAD, there was no substantial difference compared to the control group (p = 0.36). Smoking history, diabetes and dyslipidemia had a similar incidence in both groups, with no significant difference between them (p = 0.66, 0.95 and 0.56). However, heart failure and end-stage chronic kidney disease (GFR < 30 ml/min/1.73m²) were significantly more prevalent in oncologic patients’ group (p = 0.02 and 0.04).

We assessed mid-term iliac stent patency, AFS and OS for all surviving patients using Kaplan-Meier survival curves. The patency at 6 and 12 months in the oncologic group was 71.23% (95% CI: 0.49 – 0.85) and 66.48% (95% CI: 0.44 – 0.82), respectively. Patency rates were significantly higher in the control group at the same time intervals: 87.75% (95% CI: 0.75 – 0.94) and 85.66% (95% CI: 0.72 – 0.93) (Fig. 1). The one-year amputation-free survival rate was 83.36% (95% CI: 0.61 – 0.93) in group one and 95.91% (95% CI: 0.85 – 0.99) in the control group (Fig 2). The OS rate in the oncologic group at 6 and 12 months were 84% (95% CI: 0.63 – 0.94) and 80% (95% CI: 0.58 – 0.91), respectively (Fig. 3). The patients from the second group had a 100% 12-month survival rate. There was a significant difference between the two groups regarding OS, AFS and stent patency (p < 0.01).

We evaluated all postoperative complications separately for the two groups (Table 2). We noticed that patients from the oncologic group had a significantly higher incidence of postoperative thrombosis, acute myocardial infarction (AMI) and supraventricular tachycardia compared to the control group. We established a correlation between stent patency and left ventricular ejection fraction (EF), and proved that patients with diminished EF (<40%) are more likely to have occluded iliac stents at 12 months. The patency rates were notably lower in patients with impaired EF. Among patients with cancer and EF < 40%, the one-year patency rate was 33.43% (95% CI: 0.24 – 0.76), which was significantly lower compared to the rest of cancer patients, who had a patency rate of 81.81% (95% CI: 0.45 – 0.95) (p < 0.01). For the other subgroups, the one-year patency rate was 78.57% (95% CI: 0.47 – 0.93) in non-oncologic patients with impaired EF, and 88.57% (95% CI: 0.72 – 0.96) in the remaining non-oncologic patients (p = 0.05) (Fig. 4). No other relevant differences were found between the two groups regarding postoperative complications.

<table>
<thead>
<tr>
<th>Postoperative complications</th>
<th>Onco n (%)</th>
<th>Non-onco n (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>3 (12)</td>
<td>5 (10)</td>
<td>0.81</td>
</tr>
<tr>
<td>Infection</td>
<td>5 (20)</td>
<td>9 (18)</td>
<td>0.86</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>2 (8)</td>
<td>0 (0)</td>
<td>0.04</td>
</tr>
<tr>
<td>Lymphorrhagia</td>
<td>2 (8)</td>
<td>2 (4)</td>
<td>0.48</td>
</tr>
<tr>
<td>Lymphocele</td>
<td>3 (12)</td>
<td>6 (12)</td>
<td>0.97</td>
</tr>
<tr>
<td>Hypoesthesia</td>
<td>4 (16)</td>
<td>10 (20)</td>
<td>0.64</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>1 (4)</td>
<td>7 (14)</td>
<td>0.17</td>
</tr>
<tr>
<td>Oedema</td>
<td>5 (20)</td>
<td>6 (12)</td>
<td>0.37</td>
</tr>
<tr>
<td>Reperfusion injury</td>
<td>1 (4)</td>
<td>3 (6)</td>
<td>0.70</td>
</tr>
<tr>
<td>Compartment syndrome</td>
<td>1 (4)</td>
<td>0 (0)</td>
<td>0.15</td>
</tr>
<tr>
<td>Acute kidney failure</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>0.47</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>2 (8)</td>
<td>0 (0)</td>
<td>0.04</td>
</tr>
<tr>
<td>Death</td>
<td>1 (4)</td>
<td>0 (0)</td>
<td>0.15</td>
</tr>
<tr>
<td>Heparin-induced thrombocytopenia</td>
<td>0 (0)</td>
<td>2 (4)</td>
<td>0.30</td>
</tr>
<tr>
<td>Supraventricular Tachycardia</td>
<td>3 (12)</td>
<td>0 (0)</td>
<td>0.01</td>
</tr>
</tbody>
</table>
DISCUSSION

Fig. 1. Mid-term iliac stent patency of oncologic vs non-oncologic patients.

Fig. 2. Amputation-free survival for oncologic and non-oncologic patients.
Fig. 3. Overall survival in oncologic patients.

Fig. 4. Subgroup 12-month iliac stent patency rates for EF < 40%.
PAD is often overlooked in patients with cancer, mainly because it is a slow-evolving disease that can be asymptomatic in its early stages. Meanwhile, oncologic therapies are lengthy processes, which can allow PAD to progress silently to a more severe stage until it becomes abruptly symptomatic. In 2020, more than 19 million new cases of cancer were diagnosed worldwide, with an expected 47% increase in the annual number of reported cases by the year 2040. The increasing incidence of both pathologies inevitably leads to their coexistence. Unfortunately, international databases lack information on vascular surgery in oncologic patients to guide us any further.

PAD and cancer are interconnected pathologies that can influence one another. A prospective study on 6,172 subjects, analyzed the incidence of cancer in patients with vascular disease and found that PAD patients had an increased risk of developing some forms of cancer. Furthermore, patients with both PAD and an oncologic pathology have a significantly higher mortality rate. In our study, we confirmed this by observing a one-year OS difference between the two groups (p < 0.01). We also showed that oncologic patients had a significantly higher probability of developing postoperative thrombotic complications and other major life-threatening cardiovascular events. Tumour cells can trigger coagulation, and cardiovascular complications are the leading cause of death in cancer patients. This may partly explain the reduced iliac stent patency rates in oncologic patients observed in our study. Unfortunately, there are no other results regarding hybrid vascular surgery for oncologic patients at this time, and therefore, we cannot have comparative results. Almost two-thirds of our oncologic patients who did not survive reached the end of their lives with patent arteries (60%).

The impact of heart failure on the longevity of peripheral stents was already proven in international literature and our results are consistent with these data. Another overlooked factor is the psychological impact of limb loss. Between 32% and 84% of amputees have postoperative psychological disorders. Amputations can cause severe depressive states in which patients may have suicidal thoughts and/or wish for death. This amputation-induced stress is superimposed on the patients pre-existing stress, due to their history of malignancy. There are numerous other studies that connect oncological pathology with important psychological conditions such as post-traumatic stress disorder (PTSD). Avoiding amputation is crucial for these patients, many of whom have already lost all hope of a normal life. Even though the increased operative risk guides us to choose a minimally invasive option, in patients with complex arterial lesions affecting multiple anatomical levels, an intervention must be performed to address the lesions in question. Reduced invasiveness doesn’t necessarily mean better results, but it helps reduce the incidence of severe perioperative complications. Ideally, for high-risk patients, endovascular revascularization techniques should be used as the first line treatment. Patients with PAD have multiple other morbidities and, when a malignancy status is added, there is an extra reason to place them in the high-risk patient group. Unfortunately, in case of complex arterial lesions, the interventional approach is very difficult and the failure rate commensurate. Hybrid surgery is an ideal candidate for these requirements, obtaining satisfactory results for the short and medium term, this being more of an alternative to classical surgery than to endovascular techniques, especially in these situations.

Regarding intraoperative complications, there is no relevant difference in favor of oncological patients, although there is a higher incidence of postoperative thrombosis and cardiovascular events, which could also explain the reduced patency rates and OS in cancer patients. Postoperative long-term anticoagulation and antiplatelet medication could be further investigated on this matter, but at the moment there is no other evidence on prolonged anticoagulant administration or prolonged double antiplatelet therapy in cancer patients. Studies, such as the MicroTEC study (Enoxaparin Thromboprophylaxis in Cancer Patients with Elevated Tissue Factor Bearing Microparticles – identifier ClinicalTrials.gov: NCT00908960) and the PHACS study (A Study of Dalteparin Prophylaxis in High-Risk Ambulatory Cancer Patients – identifier ClinicalTrials.gov: NCT00876915), were performed in patients with malignant tumours, but were not associated with postinterventional arterial emboli in patients who underwent revascularization. We observed an inferior mid-term patency for the oncologic group following revascularization. The data obtained in our control group was consistent with data from international data bases of patients with PAD, even though patency rates are better for conventional surgery with longer lasting results. Lower patency rates for cancer patients may be due to tumoural micro emboli, which could obstruct the distal circulation, leading to an increase in peripheral vascular resistance. Increased peripheral vascular resistance has a predictive role in early graft occlusion and could lead to a reduced stent patency as well. On the other hand, oncological treatments such as chemotherapy and immunotherapy could be directly involved in the occlusion of vascular grafts and stents. Immunotherapy can cause a pro-inflammatory status with an increased level of cytokines. It has also been proven that the interruption of the programmed cell
death protein 1 (PD-1), causes an increase in the number of macrophages and T-lymphocytes that infiltrate atheromatous plaques, creating local inflammation and accelerating the atherosclerotic processes. The mechanism by which stent restenosis or occlusion occurs, in a significantly higher percentage, in patients with oncological pathology, is not yet fully elucidated and requires additional investigation.

**Conclusions**

Lower iliac stent patency rates of oncologic patients may be related to the higher incidence in thrombotic postoperative complications. It is also important to consider heart failure with reduced EF as a potential contributor to early stent occlusion, especially in patients with associated oncological pathologies.

Screening for PAD in all oncology patients could contribute to more effective disease management, while also providing less invasive treatment options before it reaches an advanced stage where such interventions are no longer viable.

Additionally, conducting further research on anticoagulant and antiplatelet therapies, specifically tailored for oncology patients, has the potential to enhance the longevity of iliac stents in this growing subgroup of patients.

**Author Contributions:**

Conceptualization, C.P. and A.C.; methodology, C.P.; software, Excel© version 2207 (Build 15427.20210); validation, V.D.C. and G.T.; formal analysis, R.H. and A.T.; investigation, C.P.; resources, A.C.; data curation, C.P. and R.H.; writing–original draft preparation, C.P.; writing–review and editing, C.P. and R.H.; visualization, A.C. and A.T.; supervision, G.T.; project administration, G.T. All the authors have read and agreed with the final version of the article.

**Compliance with Ethics Requirements:**

“The authors declare no conflict of interest regarding this article.”

“The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law: Informed consent was obtained from all the patients included in the study.”

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