Recent Developments in the Management of the Post-Thrombotic Leg and Venous Compression Syndromes

Trombotik Bacak ve Venöz Kompresyon Sendromlarının Tedavisinde Yeni Gelişmeler

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ABSTRACT Interest in and use of minimally invasive treatments in both acute and chronic deep venous pathologies is currently increasing exponentially. In cases of post-thrombotic syndrome with objective (on imaging) vein aberrations after deep vein thrombosis (DVT), endovenous percutaneous transluminal angioplasty and stenting have shown good clinical success rates with relatively high patency and low morbidity and mortality rates. Furthermore, additional interventions, such as endophlebectomy and arteriovenous fistula creation, are might be needed in case of common femoral vein involvement. In cases of venous compression syndromes without a history of DVT, even better results are obtained. This new field currently shows many interesting developments, with materials specifically designed for the deep venous system becoming available.

Key Words: Post-thrombotic syndrome; stents; venous thrombosis; cardiovascular diseases; magnetic resonance imaging; phlebography; venous thromboembolism

ÖZET Günümüzde hem akut hem de kronik derin venöz patolojilerde minimal invaziv tedavilerin kullanımı katlanarak artmaktadır. Derin ven trombozundan (DVT) sonra objektif (görüntülemede) ven aberasyonları olan post-trombotik sendrom olgularında, endovenöz pekütan luminal anjiyoplasti ve stentleme göreceli olarak yüksek açıklık ve düşük morbidite ve mortalite oranları ile iyi klinik başarı oranları göstermektedir. Ayrıca, common femoral ven tutulumu varsa, endoflebektomi ve arteriovenöz fistül oluşturulması gibi ek girişimler de gerekebilir. DVT hikayesi olmayan venöz kompresyon sendromu olgularında daha iyi sonuçlar elde edilmektedir. Bu yeni alan günümüzde, derin venöz sistem için özel olarak tasarlanmış materyaller kullanıma hazırlandıkça, birçok ilginç gelişme göstermektedir.

Anahtar Kelimeler: Posttrombotik sendrom; stentler; venöz tromboz; kalp ve damar hastalıkları; manyetik rezonans görüntüleme; flebografi; venöz tromboembolizm

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Recent insights into the management of the post-thrombotic syndrome (PTS) and other venous outflow pathologies have led to worldwide use of endovascular techniques in these disorders. PTS is a relative frequently occurring disease following acute deep venous thrombosis (DVT), most frequently of the lower extremity. DVT itself has an incidence of 1-2 per 1000 individuals annually;[1] PTS develops in 20-50% of these.[2] The most important risk factors for PTS development in DVT patients are recurrent ipsilateral thrombosis, residual obstruction or reflux after the DVT, proximal location of the thrombosis (especially at the level of

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the common femoral vein and higher up) and age.[2] Patients with PTS generally present themselves with symptoms correlated with chronic venous disease, as described in the CEAP[3], VCSS[4] and Villalta[5] scoring systems. Other important signs of PTS are venous claudication,[6] caused by impaired venous outflow, and superficial cross-over collaterals at the pubic region or lower abdomen.[7] Historically PTS has been primarily associated with deep venous reflux, caused by venous valve destruction by the reaction of the human body to the thrombus.[8,9] Recent insight however show that residual obstruction after DVT, caused by the vein wall thickening and intra-luminal webbing, is relatively more important in causing long-term pathology after DVT. Therefore the target for treatment shifted towards managing obstructive lesions. Of special note are the vein compression syndromes, especially the May-Thurner syndrome (MTS), in which abdominal veins are compressed, generally by their accompanying arteries.[10] These compressions can cause significant symptoms and complaints by their own. Moreover, by creating venous stasis, these can also be the cause of a DVT by themselves.[11]

Until recent years, PTS was managed primarily by use of compression stockings, used both preventive after a DVT (compression therapy reduces the risk for PTS development with circa 50%), and to reduce symptoms and complaints when PTS was had already been present.[12-14] Only in extraordinary cases, patients were treated surgically; i.e. creating venous bypasses (most often cross-over bypasses, called dePalma operation) or repairing/reconstructing failing deep venous valves.[15-32] In the second half of the 1990's however, the first experience with venous percutaneous transluminal angioplasty (PTA) and stenting became available.[33,34]

PTA and stenting in the circulatory system were first described by Charles Dotter and Judkins in 1964 and Palmaz et al. in 1985, respectively, and quickly gained popularity in treatment of cardiac and peripheral arterial diseases.[35,36] Already Even in 1986, papers showing use of metallic stents in the venous system were published.[37] However, because of the non-fatal nature of PTS and the fact that limb loss is very rare, interest in venous stenting lagged behind arterial use, and studies with high patient numbers were not published until recent years. Neglen en Rajuet al. were among the pioneers using who used PTA and stenting in treating thrombotic and non-thrombotic venous occlusive disease in large patient groups.[38] Others, including European and Asian authors, soon followed with their respective experience. It is of note however that at the time of writing these publications, high quality no high quality trials on this treatment have were not been performed, and most evidence is based on retrospective or prospective series.

In this article, we will give an overview of our own and other published experience in the modern management of patients with deep venous obstructive disorders.

DIAGNOSTIC WORK-UP

In our clinic, acting as a national referral center, all patient suspected of chronic deep vein obstruction receive a standardized diagnostic workup consisting of; a duplex ultrasound examination (DUS), a magnetic resonance venography (MRV),[39,40] air plethysmography (APG)[41] and a standardized intake (including CEAP,[3] VCSS[4] and Villalta[5] scoring). Baseline and control DUS are performed in all cases by the same experienced vascular technician. The caval vein and iliac veins are scanned with the patient in a supine position and the degree of obstruction (if any) is noted and the diameter of the left iliac vein is assessed at the level of the crossing of the right iliac artery to diagnose May-Thurner syndrome (Figure 1). Afterwards, the patient is asked to stand up and obstruction and reflux in the deep venous system is assessed from the common femoral vein to the tibial veins. MRV examination is performed with when the patient in supine position with a dedicated 12-element phased-array peripheral vascular coil. 10mTen mililitersL of gadofosveset trisodium, given intravenously as a single dose is used as a contrast agent. This is a blood pool agent, which remains in the vascular system relatively long, to realize achieve long scanning times. The entire inferior vena cava and bilateral venous tract, until at least the level of the infragenual

FIGURE 1: May-Thurner syndrome as imaged on 3D-venography reconstruction in a frontal, axial and lateral view.

popliteal veins, is included in the MRV scanning. APG is used to assess hemodynamic abnormalities before PTA and stenting, and control APG's are used to note any improvement in hemodynamic parameters. The APG system encompasses an air filled PTFE cuff placed around the lower leg of the patient connected to a pressure sensor, a computer translates the pressure changes within the cuff into volume changes in the lower leg. A number of quantitative hemodynamic parameters can be investigated by using APG, including; the degree of outflow, degree of venous backflow and the effectiveness of the calf-muscle pump. Clinical scoring systems are used in all patients for standardization and research purposes, and we highly encourage the creation of (inter)national registries for any type of new venous intervention. It is of note that the use of intravascular ultrasound (IVUS) to asses extend and degree of obstruction has been propagated in much of the research about venous stenting.[42] IVUS has shown to be superior in the diagnostic process of obstructive venous disease, especially compared to single plane venography. In our experience however a combination of pre-operative MRV and peri-operative multiplanar venography and cone-beam CT are more than adequate to diagnose venous obstructive disease, plan and evaluate the intervention.

PTA AND STENTING PROCEDURE

After preoperative planning based on MRV and DUS findings, patients are admitted to our hospital for the recanalization procedure, which is performed under local analgesia in some cases of sole extraluminal vein compression (i.e. MTS) or general anesthesia in most cases of post-thrombotic disease or external compression syndromes. In cases of extensive obstruction in the common femoral vein, insufficient inflow into iliac segments can be expected; in these cases we perform an endophlebectomy of the CFV with or without an AV-fistula to improve patency during follow-up. The stenting procedure itself encompasses the cannulation of either the popliteal or the femoral vein under DUS guidance. A 5F sheath is then introduced and an antegrade venogram is made to assess extend and localization of the venous obstruction (Figure 2). By use of various stiff guide wires the obstruction is then passed, this might be technically difficult in cases of extensive post-thrombotic disease; however in our experience it is possible in almost all ca-

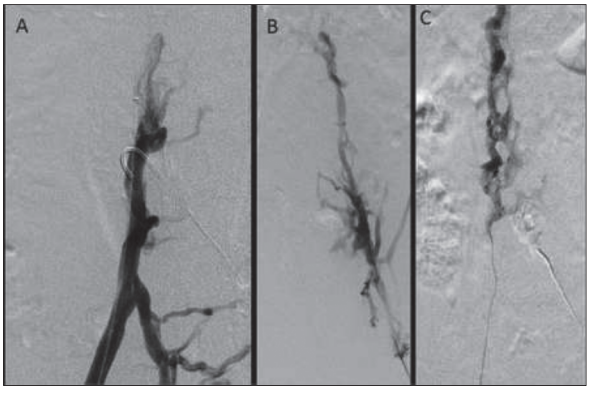

FIGURE 2: Bilateral post-thrombotic obstruction in the right (A), left (B) and inferior caval vein (C).

ses (>95%). Following the crossing of the obstruction, the affected vein segments are pre-dilated with 8-14 x 40 mm balloon catheters. One or more self-expendable stents are then placed over the affected segments. Stent sizing is based on the diameter of the vessel and we oversize the stents by approximately 20% to prevent stent migration. Following stent placement the treated segments are dilated again by balloon angioplasty. The final control venography is then performed (Figures 3 and 4). In case of a successful procedure one expects to see contrast outflow through the stented segment and no contrast filling the collaterals. Post-operatively patients are anticoagulated for a period of at least 5 days with LMWH's, during which anticoagulation with vitamin K antagonist is started. This is continued for at least 6 months, aiming at an INR of 2.5-3.5. Recently we have started using the new oral anticoagulants, i.e. Rivaroxaban and Dabigatran, in some patients instead of coumarines. Patients are generally discharged within 48 hours after intervention, and visit our outpatient clinic at regular intervals.

ENDOPHLEBECTOMY AND ARTERIOVENOUS FISTULA CREATION

The endophlebectomy is performed in patients in whom the future inflow, after stent placement, is predicted to be too low to guarantee long-term patency. This is done by careful examination of duplex, MRV and venography findings in a multidisciplinary team. The goal is to create one major lumen in a vein who's lumen is generally divided into multiple smaller lumens by the intravenous webs and trabeculae. Via an incision in the patients groin the diseased common femoral vein is carefully exposed. A longitudinal venectomy is performed. Flow from the iliofemoral tract proximally and distally from the venectomy is controlled as well as from the major side branches. Any fibrotic residue is meticulously removed from the lumen. Care must be taken to leave an adequate vein wall. Afterwards the venectomy is closed either primarily or with a patch.

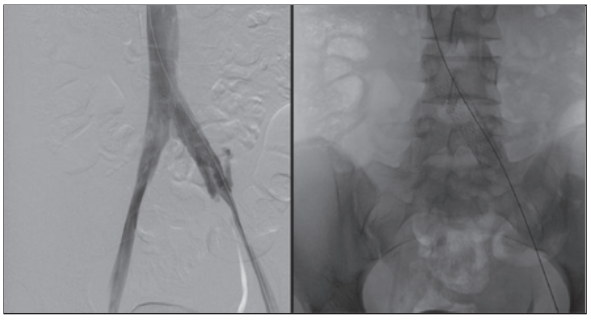

FIGURE 3: May-Thurner syndrome treated by placement of a dedicated venous stent in the common iliac vein (left - last control venography; right – control plain X-ray).

FIGURE 4: Bilateral and caval post-thrombotic obstruction treated by placement of a multiple venous stent in the inferior caval vein and both iliac tracts (left - last control venography; right – control plain X-ray).

Arteriovenous fistula a generally created in the same session as the endophlebectomy is performed. In our experience, the use of a small polytetrafluoroethylene (PTFE) loop between the common femoral vein and artery is superior to direct site-to-site fistula or the use of a native vessel. One of the most important considerations for this is the fact that these fistulas can be easily occluded by use of endovascular techniques.

TECHNICAL RESULTS AND CLINICAL OUTCOME

Technical success rates of deep venous PTA and stenting described in literature are well above 90%, generally approaching 100 percent% depending on studies and patient population. In our own experi-

ence patency rates are 74%, 81% and 96% respectively, for primary, assisted primary and secondary patencypatencies, in a population with 14% primary and 86% secondary deep venous obstructions (n=63).[43] Neglén et al. showed a clear difference between primary and secondary disease; 79% primary and 100% secondary patency in primary disease (N=518), and 57% primary and 86% secondary patency in secondary disease (N=464).[38] Ulcer healing rate was circa 60% in Neglén's combined population and ulcer recurrence rate was 8%. Other authors have reported on similar patency and ulcer healing rates.[33,44,45]

COMPLICATIONS

Theoretically the most feared complication of this type of intervention would be a (fatal) pulmonary embolism. In our experience and available articles this however has never occurred, and deep venous recanalisation can be considered a relatively safe procedure. The most important complication in these patients is the occlusion of the stented tract by thrombus. Therefore it is of the utmost importance to adequately anticoagulate these patients peri-operatively by use of heparin or heparin-like substances. In our experience, 4% of treated patients developed an immediate re-occlusion during the procedure, which was immediately treated.[43] Moreover, 11% developed re-occlusion the day after treatment, these were treated with catheter directed thrombolysis, secondary PTA and stenting, surgical thrombectomy and arteriovenous fistula creation.[43] Other procedure- related complications included mostly minor hemorrhages at the puncture site (10%).[43] Post-procedure patients receive a standard regimen of LMWH's low molecular weight heparins for a number of days, during which vitamin K antagonist treatment is started and continued for at least 6 months in our center (the method and length of anticoagulation post-stenting however is an issue currently under debate).

NEW DEVELOPMENTS

It is of note that in current literature on stenting techniques rely on arterial stents placed in the venous system. Ideally however, venous stents are characterized by a higher flexibility and radial force. In many articles, stenting is performed by use of braided stainless steel stents, like the Wall stent (Boston Scientific, Galway, Ireland). By nature of their design these stents have a relatively high tendency to increase in diameter and shorten, and thereby showing tapering at the end,. Moreover these stents are somewhat rigid, which can be viewed as suboptimal in a delicate system like the venous tract. We therefore preferred use of nitinol stents with great diameters. In our earlier experience, this included the Sinus XL stent (Optimed, Ettlingen, Germany), a stent with high radial force and adequate diameters available. However this stent was also rigid. At the time of writing new stents have become available, specifically aimed at the venous system, like the Zilver vena stent from Cook Medical[46] and the Optimed Sinus Venous. These stents are available in adequate lengths and diameters to treat venous lesions (which are generally found over a longer location). Furthermore, these stents are characterized by high radial force and are very flexible compared to older stent designs. It is our- We hope that these new materials will increase clinical success rates and simplify treatment techniques.

CONCLUSION

Interest in and use of minimally invasive treatment in both acute and chronic deep venous pathology is currently increasing exponentially. In cases of PTS with objective (on imaging) vein aberrations post-after DVT, endovenous PTA and stenting have shown have shown good clinical success rates with relatively high patency and low morbidity and mortality ratesgood clinical success rates, with relatively high patency rates and low morbidity and mortality. In cases of venous compression syndromes, without a history of DVT, even better results are obtained. This new field currently shows many interesting developments, with materials specifically designed for the deep venous system becoming available.

Conflict of Interest

Authors declared no conflict of interest or financial support.

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