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Journal of Bionic Memory Original article

Carotid artery stenting with or without distal filter-type embolic protection device: A single center experience

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ABSTRACT

Aim: To share the data of patients who underwent carotid artery stenting (CAS) with or without a distal filter-type (DF) embolic protection device (EPD) in our clinic and our own experiences.

Method: The files of patients who underwent CAS in our clinic between November 2019 and January 2021 were reviewed retrospectively. Patients with >50% stenosis in symptomatic patients, >70% in asymptomatic patients, and those who had CAS at least 48 hours after the last symptom were included. Patients who underwent acute CAS and were treated for restenosis after carotid stent or endarterectomy were excluded from the study. Thirty-five patients who used DF in CAS procedure and 16 patients who did not use EPD were included in the study.

Results: No significant difference was found between the two groups in terms of new neurological and cardiac vascular events *(p=0.58)*. A new ischemic lesion was detected in diffusion MRI in 76.5% of the patients who underwent CAS using a DF type EPD and 81.8% of patients who underwent CAS without the use of an EPD. No significant difference was found between the detection rates of new ischemic lesions *(p=0.73)*.

Conclusions: Since we found no significant difference in neurological and cardiac vascular events between the patients who underwent CAS with and without use of DF type EPD, we suggest that CAS can be performed without the use of a DF type EPD in suitable patients to reduce the cost of the procedure.

Key words: Carotid artery stenting, embolic protection device, distal filter, stroke, carotid artery stenosis.

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Introduction

Carotid artery stenting (CAS) is a long-established treatment for symptomatic and asymptomatic carotid stenosis. Currently, guidelines recommend CAS as an alternative treatment to carotid endarterectomy (CEA) operation in centers with a complication rate of less than 6% in symptomatic carotid stenosis and less than 3% in asymptomatic carotid stenosis [1]. It is known that in CAS, compared to CEA operations, the frequency of minor stroke is increased while the risk of myocardial infarction risk is decreased. No significant difference was found in terms of major ischemic events [2-4]. The advantages of CAS treatment compared to CEA are that it does not involve surgical incisions, there is no need for general anesthesia, there is no risk of cranial nerve damage, and cerebral perfusion can continue during the procedure in patients with contralateral stenosis and insufficient collateral flow through the Willis polygon [5]. The most

prominent disadvantage is the risk of distal embolism at all stages of the procedure, such as crossing the stenosis with microwire, stent placement and angioplasty. Several embolic protection devices (EPD) have been produced and used to reduce the risk of distal embolism. Embolic protection devices are classified as distal occlusion balloons, distal filters (DF), and proximal occlusion devices (POD). Combined EPD applications are also available [5]. Many centers practice CAS procedure with EPDs. DF type embolic protection devices are the most widely used group in daily practice. While previous studies have reported that the risk of stroke is lower in patients with EPD; there are also publications reporting that there is no significant difference in risk of stroke, transient ischemic attack (TIA), and death between patients with and without EPD [6-9].

In this study, we wanted to share our experience and the data of our patients who underwent CAS with DF type EPD or without EPD in our center.

Materials and Methods

In this study, patient files who underwent CAS treatment between November 2019 and January 2021 in the comprehensive stroke center clinic of Abant Izzet Baysal Training and Research Hospital were retrospectively reviewed from hospital archive.

Patients included in this study were over 18 years of age, underwent CAS procedure within 48 hours of last symptom and had stenosis in carotid artery: according to North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria >50% stenosis in symptomatic patients and >70% stenosis in asymptomatic patients [10]. Patients who underwent acute CAS and were treated for old carotid stent or endarterectomy restenosis were excluded from this study. Out of 74 patients who underwent CAS in our clinic between the specified dates, 51 patients met our criteria and had their data analyzed (Figure 1).

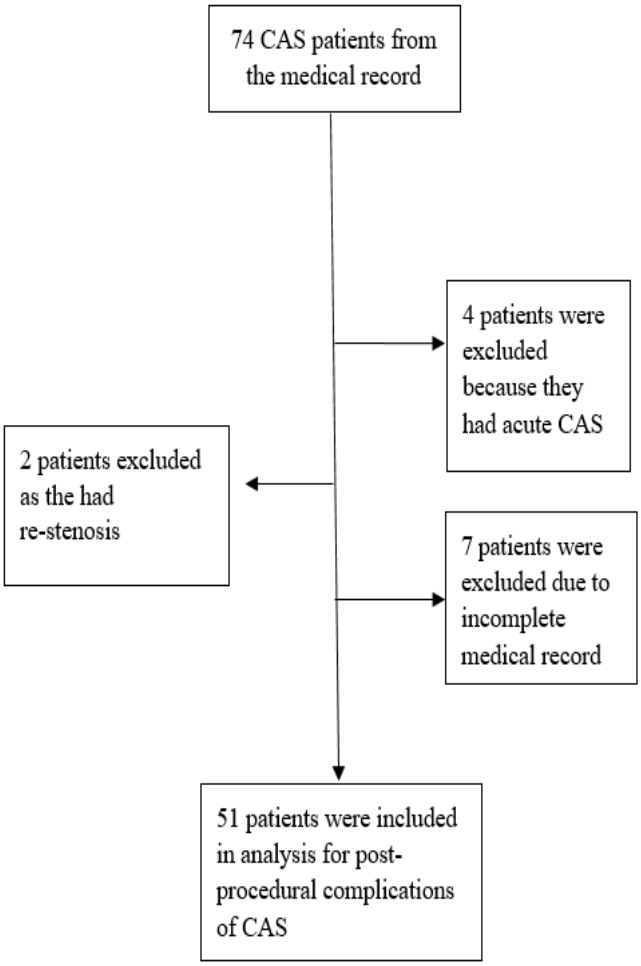

Figure 1. Flow chart.

CAS procedure

Patients received at least 5 days of Acetylsalicylic acid (ASA) 100 mg/day and Clopidogrel 75 mg/day or ASA 100 mg/day and Ticagrelor 90mg 2x1 treatments before undergoing the procedure. A 6F guide catheter over an 8F femoral sheath was used in the procedure. Patients were heparinized at a dose of 50/U kg to obtain activated clotting time within the therapeutic range. After the diagnostic angiography, stenosis measurements were made and symptomatic patients with >50% stenosis and asymptomatic patients with >70% stenosis underwent CAS procedure.

Protege (Medtronic Corp.; Minneapolis, MN, USA) stent was used in all patients. During the procedure, pre-dilatation was performed in patients who did not have an opening through which the stent could pass, and post-dilatation was performed in patients with >30% residual stenosis at the end of the procedure. The use of an EPD is also left to the operator's decision.

The data of 35 patients who underwent CAS with DF and 16 patients who underwent CAS without EPD were evaluated. Vascular risk factors of the patients, technical data related to the procedure, periprocedural complications, and cerebral and cardiac vascular events were noted. Imaging of 17 patients from the DF group and 11 patients from the group without EPD who had 1.5 T diffusion magnetic resonance imaging (MRI) (Signa Explorer, GE Healthcare, Chicago, IL, USA) before and in the first 24 hours after the procedure were evaluated. Newly developed ischemic lesions with a size of <1 cm are indicated numerically. Patients with an infarct larger than one cm are noted as well. All patients were seen at the first month and third month follow-ups, and any newly developed cardiac and cerebral vascular events were noted and were evaluated for restenosis with Doppler USG. Primary outcome was determined as stroke and myocardial infarction whereas secondary outcome was determined as detection of a new ischemic lesion in diffusion MRI and increased number of ischemic lesions.

The study was approved by the Ethics Committee of Abant Izzet Baysal University. (02/03/2021, 79). After that, informed consent forms were obtained from the patients or their first-degree relatives, and then the data were evaluated.

Statistical method

Data were evaluated with SPSS 21.0 (IBM Corp.; Armonk, NY, USA) program. Qualitative variables were expressed as numbers and percentages whereas quantitative variables were expressed as mean ±SD. Quantitative variables with normal distribution between two independent groups were evaluated with the Independent Sample t test, and variables without normal distribution were evaluated with the Mann Whitney U test. Chi-square test was used when comparing categorical variables. A P value of <0.05 was considered statistically significant.

Results

The mean age of the patients within the DF group was 69±8.8 (range; 50-90) years, and the mean age of the patients in the group without EPD was 70±8.6 (range; 54-83) years (p=0.48). There were 27 male (77.1%) and 8 female (22.9%) patients in the DF group and 12 male (75%) and 4 female (25%) patients in the group without EPD. There was no significant difference between the two groups in terms of age and gender (p 0.48, 0.86, respectively). Hypertension (HT) was significantly more common in patients who did not use an EPD (p=0.01). There was no significant difference between the two groups in terms of the frequency of diabetes mellitus (DM), hyperlipidemia (HL) and coronary artery disease (CAD) (Table 1).

Out of 35 patients in the DF group, 31 (88.6%) received ASA 100 mg/day + Clopidogrel 75 mg treatment whereas the remaining 4 (%11.4) received ASA 100 mg/day + ticagrelor treatment. In the group without EPD, 15(%93.8) patients received ASA 100 mg/day + clopidogrel 75 mg treatment and 1 (%6.3) patient received ASA + ticagrelor treatment.

In the DF group, 5 (14.3%) of the patients who underwent CAS had asymptomatic ICA stenosis compared to 3 (18.8%) in the group

without EPD. There was no significant difference between the ratios of symptomatic and asymptomatic patients between the two groups (p=0.69). In DF group, stents are placed to the right ICA of 16 patients and left ICA of 19 patients. In the group without EPD, 7 patients had their right ICA stented whereas 9 patients had their left ICA stented.

Table 1. Comparison of patients' demographic data and vascular risk factors.

Parameters	DF Group n=35	Group Without EPD n=16	*p*
Age (year)±SD	69±8,8	70,9±8,6	*0,48 **
Gender (n, %), (Male/Female)	27 (77.1) / 8 (22.9)	12 (75) / 4 (25)	*0,86***
HT (n, %)	23 (65.7)	16 (100)	*0,01 ***
DM (n, %)	18 (51.4)	8 (50)	*0,92 ***
HL (n, %)	25 (71.4)	11(68.8)	*0,84***
CAD (n, %)	13 (37.1)	9 (56,3)	*0,20 ***

**Independent samples t test, ** Chi square test, DF: Distal filter, EPD: Embolic protection device, CAD: Coronary artery disease, DM : Diabetes mellitus, HL : Hyperlipidemia, SD: standard deviation*

Balloon angioplasty was performed in 22 patients (%62.9) from the DF group. Only pre-dilatation was applied to 7 patients (20%), only post-dilatation was applied to 8 patients (22.9%), and both were applied to 7 patients (20%). Balloon angioplasty was performed in 13 patients (81.3%) from the group without an EPD. Two patients (12.5%) underwent pre-dilatation whereas 11 (68.8%) patients underwent post-dilatation. There was no significant difference in balloon angioplasty application ratios between the two groups (p=0.18). The mean residual stenosis rates were detected as 13.4±10.5 (range, 0-32) in the DF group and 15.4±10.6 (range, 0-40) in the group without EPD. There was no significant difference between residual stenosis rates (p=0.53), (Table 2).

Table 2. Comparison of data on CAS.

Parameters	DF Group n=35	Group Without EPD n=16	*p*
Symptomatic/ Asymptomatic (n, %)	30 (85,7) / 5 (14,3)	13(81,2) / 3 (18,8)	*0,69*
Right/ Left (n, %)	16(45,7) / 19(54,3)	7 (43,8) / 9 (56,3)	*0,89*
Stenosis rate (%) ±SD (min-max)	77,2±10 (57-95)	67,7±10,6 (55-95)	*0,11*
Contralateral ICA stenosis rate (%) ±SD (min-max)	27,7±35,3 (0-100)	16,7±16,1 (0-50)	*0,25*
Arcus type 1/2/3 (n, %)	8 (22,9) / 24 (68,6) / 3 (8,6)	3 (18,8) / 7 (43,8) / 6 (37,5)	*0,05*
Residual Stenosis (%) ±SD (min-max)	13,4±10,5 (0-32)	15,4±10,6 (0-40)	*0,53*
Angioplasty rate (%)	62,9	81,3	*0,18*

DF: Distal filter, EPD: Embolic protection device

One patient in the DF group developed myocardial infarction 24 hours after the procedure and coronary stenting was performed by the cardiologist. Again, one patient in the DF group developed stent thrombosis during the procedure. The patient with total occlusion of the contralateral ICA was taken to acute endovascular recanalization and recanalization was achieved. However, the patient who developed a large bihemispheric infarct died on the 5th day of the procedure. In the group without EPD, TIA was detected in one patient and a minor stroke without disability was detected in another. There was no significant difference between the two groups in terms of new neurological and cardiovascular events (p=0.58). Three (8.6%) of the patients in DF group had vasospasm advanced enough to require vasodilator admission while the patients in EPD had no such problem (Table 3).

Table 3. Periprocedural vascular complications.

Parameters	DF Group	Group Without EPD	*p*
Vasospasm (require vasodilator) (n, %)	3 (8,6)	0	
TIA (n, %)	0	1 (6,3)	
Minor stroke (n, %)	0	1 (6,3)	
Stroke (n, %)	1 (2,9)	0	
Myocardial infarction (n, %)	1 (2,9)	0	
Stent thrombosis (n, %)	1 (2,9)	0	
Mortality (n, %)	1 (2,9)	0	
Cardiac and cerebral vascular event (n, %)	2 (5,7)	2 (12,5)	*0,58*

DF: Distal filter, EPD: Embolic ptotection device, TIA: Transient ischemic attack

Table 4. Diffusion MRI findings.

Parameters	DF Group n=17	Group Without EPD n=11	*p*
New ischemic lesion (%)	76,5	81.8	*0,73*
Number of new lesions ±SD	3,8±5,6	5,2±7,6	*0,61*
Ipsilateral new lesion (%)	76,5	72,7	
Number of ipsilateral new lesions ±SD	3,6±5,7	4,6±7,8	*0,94*
Contralateral new lesion (%)	17,6	18,2	
Number of contralateral new lesions ±SD	0,1±0,5	0,2±0,6	*0,82*
Posterior circulation new lesion (%)	5,9	9,1	
Number of posterior circulation new lesions ±SD	0	0,3±0,9	*0,45* **

MRI: Magnetic resonance imaging, DF: Distal filter, EPD: Embolic protection device,

Seventeen patients in the DF group and 11 patients in the group without EPD had diffusion MRI examinations before the procedure and within 24 hours after the procedure. When the imaging of these patients was evaluated, new ischemic lesions were detected in 13 patients (76.5%) from the DF group and 9 patients (81.8%) from the group without EPD. The mean number of new <1 cm ischemic lesions in diffusion MRI was 3.8±5.6 in the DF group and 5.2±7.6 in the group without EPD. There was no significant difference in the number of new ischemic lesions observed in diffusion MRI and the rates of detection of new lesions between the two groups (p 0.61, 0.73, respectively) (Table 4).

Discussion

In clinical practice, embolic protection devices are used in many centers, and DF type devices are the most widely used ones. Although embolic protection devices are extensively used, there are still authors who are skeptical about their effectiveness. According to the European Society for Vascular Surgery (ESVS) guideline [10], the use of EPD should be considered in patients undergoing CAS with a recommendation of Class IIa, Level B [11].

While there are publications in the literature reporting that the risk of stroke is lower in patients who use EPD during CAS procedure, there are also publications reporting that there is no significant difference between patients with and without EPD, and that new ischemic lesions are more common in patients who use EPD [7-9, 12-14].

In the randomized controlled study reported by Barbato et al. in which patients who underwent CAS with and without DF, diffusion MRI examination revealed that the new ischemic lesions were detected in 72% of the patients using DF and in 44% of the patients without

EPD. There was no significant difference between the two groups. [7]. In a randomized study conducted by Macdonald et al., new ischemic lesions were found 24 hours after the procedure in the diffusion MRI of 29% of the patients who used DF and in 18% of patients in the group without EPD. The number of microembolic signals detected by transcranial Doppler USG during the procedure was found to be significantly higher in patients with DF [13]. In our study, no significant difference was found between the rates of new ischemic lesions in diffusion MRI examinations between patients with and without DF.

In the subgroup analysis of the Pro-CAS study reported by Theiss et al., no significant difference was found in mortality and stroke between 3543 patients with EPD and 1166 patients without EPD [13]. In a subgroup analysis evaluating patients in the CAS leg of the Multicenter International Carotid Stenting Study (ICSS), reported by Doig et al., major cardiac and cerebrovascular events within the first month were found in 8.5% of patients with EPD while they were found in 4.6% of the group without EPD; however, in terms of major cardiac and cerebrovascular events no significant difference was observed between the two groups [8]. In a meta-analysis study by Garg et al., stroke risk was found to be significantly lower in patients using EPD compared to patients not using EPD [9]. In a study by Knappich et al., in which the data of 13086 CAS cases were evaluated retrospectively, a significant reduction in the rate of stroke, mortality and duration of hospital stay was found with the use of EPD [12]. In a meta-analysis study, the number of new ischemic lesions detected was found to be significantly lower in patients who used EPD (33%) compared to the group that did not (45%) [14]. In our study, however, no significant difference was found between the two groups in terms of cardiac and cerebral vascular events. There was also no significant difference in terms of newly developed silent ischemic lesions.

In a study by Binning et al., CAS was performed without EPD in 174 patients and none of the patients developed neurological complications. In this study, post-dilatation was avoided, considering that distal emboli most likely develop during this phase. Despite this, the rate of restenosis requiring intervention in the follow-up of patients (2.8%) remained low [16]. In our study, post-dilatation was performed when residual stenosis over 30% was detected in patients. The reason for the relatively high presence of silent infarcts we found in our patients may be that the rate of total angioplasty was 68% and the rate of post-dilatation was 50%. While there are publications stating that PODs reduce the risk of embolism more than DF, there are also publications with a large number of cases reporting that there is no difference between them [17-19]. In the randomized study reported by Aytac et al. in which new ischemic lesions detected in post-procedure diffusion MRI examination were compared, new ischemic lesions were found at a rate of 65.4% in the DF group compared to 47.4% in those using POD, and no significant difference was observed [15]. In a meta-analysis comparing patients with POD or DF, Texakalidis et al. reported no significant difference in terms of mortality, TIA, and stroke risk [20]. In a randomized study reported by Montorsi et al., in which patients using randomized POD or DF, microembolic signals were evaluated with transcranial Doppler USG during the procedure and the number of MES was found to be significantly lower in those using POD [21]. POD was not used in our study. When the literature is

reviewed, it is noteworthy that they are generally more successful than DFs in preventing silent ischemic lesions. [17, 19-21]

Although CAS treatment has been in use for a long time, it is not possible to give a clear answer as to whether the use of EPD is necessary. There are conflicting results in studies investigating microembolic signals with transcranial doppler and post-operative new ischemic lesions with diffusion MRI. When evaluated in terms of clinically manifesting major embolic events, no significant difference was found in general [6-9, 12-13]. In our patients too, no difference was found between the two groups in the number of neurological and cardiovascular events or new ischemic lesions in diffusion MRI.

The advantages of our study are that silent infarcts were evaluated by imaging and the use of the same stent and DF in all patients. The disadvantages of our study are that the study was single-centered, the number of patients included in the study was small, diffusion MRI examination could not be performed in all patients, and the study was conducted in a retrospective nature.

Conclusion

While looking for an answer to the question of how to achieve embolic protection, it is necessary to evaluate many parameters such as collateral status, vascular tortuosity, stenosis rate, plaque morphology and make a choice according to the patient. We suggest that CAS can be performed without using DF, especially in patients who are thought to be unlikely to undergo pre-dilatation or post-dilatation considering pre-procedural radiological images and angiography imaging. While there is no change in the clinical outcome of the patients, the cost of the procedure can be reduced in this way. The answer to the questions of whether an EPD should be used and if so, what type should be used can only be possible with randomized controlled studies with a large number of cases comparing proximal protective devices, distal protective devices, combined method with each other.

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Journal of Bionic Memory **Review article**

Biliary stents: models and advancements

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ABSTRACT

Obesity and sedentary lifestyle increase the formation of stones in the biliary tract. Choledochal stent placement with endoscopic intervention in cases of choledochal stones and bile leakage has been a common procedure in gastroenterology practice in recent years. Intervention for post-op biliary strictures is increasing in parallel with the number of liver transplantations. Stent placement procedures for palliation of primary or metastatic malignant processes of the biliary tract also contribute to the comfort of life of patients. In this article, brief information about the stents used in the biliary system is presented.

Key words: Biliary drainage, plastic stent, metallic stent, jaundice, cholestasis.

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Introduction

The common bile duct is responsible of flow of the bile that produced in the liver to the duodenum. Jaundice occurs when bile cannot flow into the duodenum due to stasis or obstruction. Stent placement in the common bile duct provides palliative or permanent treatment in addition to treatment for the underlying etiology in patients with obstructive jaundice.

The process of placing lumen tubes in the bile ducts in order to eliminate bile stasis in the biliary tree is called stenting. Failure to resolve bile stasis carries the risk of hepatocellular insufficiency, cholangitis and biliary cirrhosis.

Techniques such as Whipple operation or hepaticojejunostomy, choledochojejunostomy cholecystojejunostomy have been used in the past to overcome biliary obstruction. In parallel with the advances in endoscopic interventions, biliary stenting has taken the first place in eliminating biliary stasis, instead of surgical techniques.

Stents are inserted by endoscopic retrograde cholangiopancreatography (ERCP) by passing through the working channel of the duodenoscope and their removal is with the same method. In cases where the endoscopic method cannot be used, internal or external biliary drainage stents can be inserted externally with the percutaneous transhepatic cholangiography method [1].

Lumen tubes placed in the bile ducts are classified as plastic or metal stents according to the material they are manufactured from.

Plastic biliary stents

These stents are produced in different diameters, lengths and shapes from polyurethane, polyethylene and their mixtures of plastic materials. Stent diameters are expressed in french (Fr) corresponding to 1/3 of centimeter. Plastic stents can be 3-12 Fr in diameter and 1-25 cm in length. They are

manufactured as straight at both ends (Amsterdam type, Figure 1), curved at both

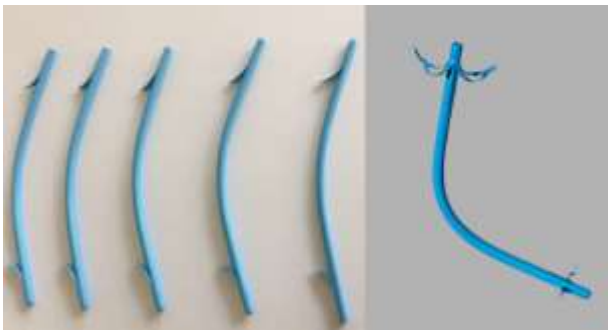

Figure 1. Plastic biliary stent (Amsterdam type).

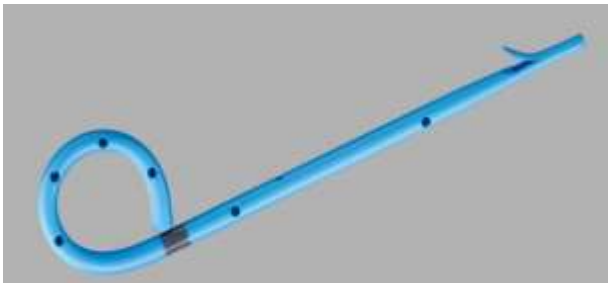

Figure 2. Plastic pigtail biliary stent.

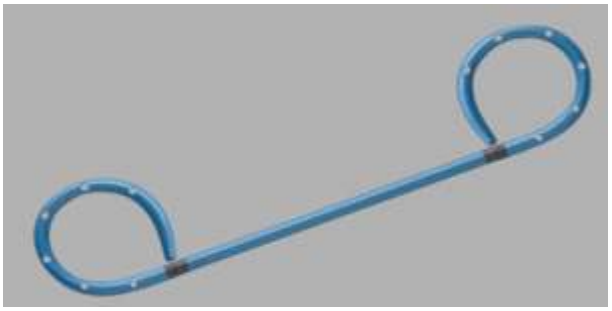

Figure 3. Plastic double pigtail biliary stent.

ends (double pigtail, Figure 2) or as a straight end and pigtail at one end, depending on the place and purpose of use (Figure 3). It has single or multiple flaps at both ends to prevent migration from the lumen.

In patients with gallbladder stones or biliary sludge associated with choledoc stones, plastic stenting is performed on difficult/large/multiple choledoc stones that cannot be completely removed by ERCP after the choledoc stones are removed. In patients with benign biliary stenosis, stenting is performed to maintain the lumen patency after dilation. In addition, plastic stenting suitable for the diameter of the common bile duct is applied to patients with post-op biliary leakage. Stent is applied after removal of ascaris lumbricoides and fasciola hepatica parasites that rarely cause biliary obstruction. The use of plastic stents is limited in biliary strictures secondary to malignant etiology.

Plastic stents can also be placed in the pancreatic duct. The most common indications for pancreatic stenting include; pancreatitis prophylaxis after ERCP procedure, chronic obstructive pancreatitis and congenital variation of the pancreatic duct. Pancreatic stents are used in the canal with flat ends, relatively smaller diameters and short lengths.

The most common complication in patients with plastic stent placement is stent migration and obstruction. Less frequently, it may cause pancreatitis, cholangitis, cholecystitis, and intestinal perforation [2].

Metallic stents

Self-expanding metal stent (SEMS) are reduced in diameter to pass through the working channel of the duodenoscope and reach a certain lumen opening when released. They are generally made of nitinol. Nitinol, an alloy of nickel and titanium, is a tissue-lumen compatible radio-opaque material. In addition, steel and nitinol-coated platinum (platinol) are also used in stent construction. They are primarily preferred in malignant diseases of the biliary tree. Metallic stenting is performed in the palliation of jaundice secondary to cholangiocarcinoma, gallbladder, pancreas, ampulla of water, liver cancer and metastatic biliary tract tumors [3, 4]. They promise a wider and longer lumen opening compared to plastic stents [5].

Post-operative biliary strictures are cases where both types of stents are used alone or in combination. The use of stents in the treatment of strictural complications after liver transplantation has increased in parallel with the number of transplantations in recent years [6].

Metal stents can be of different diameter (6-12mm), length (4-12 cm), shape and structure depending on the localization and stenting indication. Hook and cross, hand woven were produced in different architectural structures in order to expand and provide lumen opening. There are metal stents with partial or full coverage (Figure 5) as well as uncovered (Figure 4).

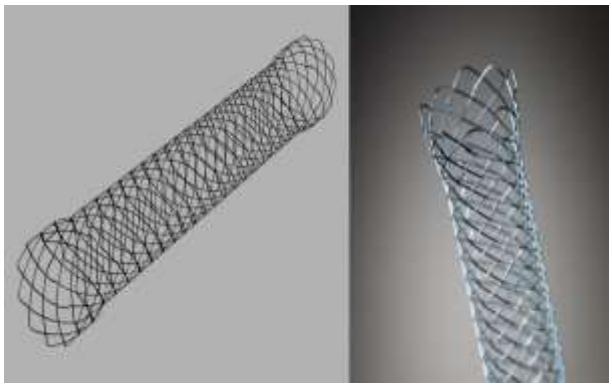

Figure 4. Uncovered self-expandable metallic stent.

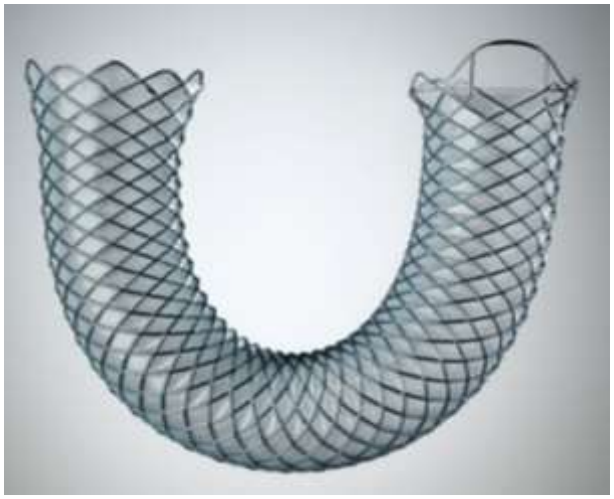

Figure 5. Full covered self-expandable metallic stent.

Stent models covered with silicon material fully or partially are preferred in order to prevent tumor growth in malignant processes. Polyether polyurethane, polyurethane, polytetrafluoroethylene fluorinated ethylene propylene or polycaprolactone materials are also used as metal stent covering material. There are publications stating that there is no difference between coated metal stents and uncoated metal stents in terms of luminal patency and occlusion [7]. Covered metal stents are easier to remove when needed than uncapped ones, unfortunately, they are more likely to migrate than uncapped stents.

Metallic stents end slightly widened to prevent migration (dumbbell appearance). Y-shaped types are also available to be placed in the intrahepatic bifurcation area. Metallic stents are incomparably more expensive (50-60 times) than plastic stents. It is recommended for patients with a life expectancy longer than 4-5 months [8]. In addition, it is used in selected cases because the risks of cholangitis, occlusion and re-endoscopic intervention are more advantageous than plastic stents [9]. Occlusion due to migration and tumor ingrowth are the main disadvantages of metallic stents. Luminal occlusions can be temporarily overcome by placing another stent with a narrower diameter inside the stent.

While bile sludge, bile stasis, contact of bile with a foreign surface and bacteria facilitate stent lumen obstruction [10-12], coating the inner lumen with perfluoroalkoxyl or a different material and adding an anti-reflux valve mechanism may delay the occlusion of the stents [13] . Silver coating of metallic stents may prolong the luminal opening [14]. Antibiotic-containing stents and biodegradable stents are stents produced as a result of different searches [15]. Magnetic stents are experimental stents that are easily removed without the need

for endoscopy by advancing outside the body. Stents that release chemotherapeutic or radioactive I^{125} may contribute to the treatment of the underlying disease in cases of malignancy, together with existing chemotherapy drugs [16, 17] .

Conclusion

Stents contribute to palliation in hepatobiliary malignancies, including those without surgical intervention. With the developing endoscopic techniques, more stenting options will emerge, which will force developments in stenting.

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Port catheters: Indications, complications and quality of life

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ABSTRACT

Port catheters are very critical component in the care of patients with chronic diseases such as cancer that require frequent hospitalization and venous access. Because port catheters can be used for biochemical analysis of blood, administration of chemotherapeutic agents, transfusion of blood and blood products, fluid and antibiotic support, and total parenteral nutrition. Port catheters can be placed safely and easily under ultrasound guidance. Port catheters, whose early or late complications are rarely seen, provide a significant improvement in the quality of life of patients compared to other venous access catheters.

Key words: Antineoplastic agents, catheterization, ports catheters, adverse effects, quality of life.

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Introduction

Intravenous access is often required for biochemical blood analysis and treatments of patients admitted to the hospital. This access is often via peripheral venous catheterization. However, central venous access is required in patients who need intensive treatment for central venous pressure monitoring, fluid replacement, long-term total parenteral nutrition, blood and blood product transfusion, drug administration (especially chemotherapeutic drugs). It is the procedure of placing a catheter in a vein that joins the heart directly [1].

The use of central venous catheters goes back to 1929, when Werner Forssman used a plastic cannula from the peripheral arm vein to the heart [2]. Access to the subclavian vein was described in 1952 for central venous access [3]. Silicon-based catheters were started to be used by Broviac in 1973 and Hickman in 1977 [4]. Since 1982, implantable venous access systems have been used instead of peripheral venous vessels in situations requiring repetitive blood collection and regarded as a suitable method to administrate drugs used in cancer therapy [5].

Central venous catheters

Central venous access can be performed by a central venous catheter or peripherally inserted central catheter. There is no clear superiority of any procedure type, central venous catheter or peripherally inserted central catheter, for venous access [6].Nowadays non-tunneled central venous catheters, tunneled central venous catheters and subcutaneously implanted ports are used for central venous access [7].

Non-tunneled central venous catheters

It is used in patients whose condition is unstable, require hemodynamic monitoring, acute care, need high volume fluid replacement, multiple therapy, blood and blood product transfusion and parenteral nutrition, by

providing access to the internal jugular vein and need treatment for 14 days or less [8]. Antimicrobial non-tunnelled catheters are often used for these critical patients to reduce the risk of infection by approximately 40% [9].

Tunneled central venous catheters

It is placed subcutaneously in the jugular or subclavian vein. These catheters are used for patients who need vesicant and irritant treatment for 31 days or longer, and are administered parenteral nutrition or chemotherapeutic agents. These catheters can be used especially if patients need to be hospitalized for longer than 15 days [10].

Ports catheters

Ports catheters provide a safe access route for administering blood collection, therapeutic purposes, including chemotherapy, parenteral nutrition, blood transfusions for biochemical analysis without impairing or minimally affecting patients' life quality [11]. Port catheters are often used for patients who require long-term central venous access. It is especially recommended if there is a need for intermittent or cyclic infusion treatment for 6 months or longer [8, 12].

Who should place the port catheters?

While port catheter placement was previously performed under general anesthesia, nowadays it is easily performed using ultrasonographic and fluoroscopy imaging methods by interventional radiology with intravenous sedation (midazolam/fentanyl) in a safe, effective and rapid way [13].

In one study, it was found that port catheters placed by general surgeons and interventional radiologists had similar complication rates. Nevertheless, when hospital costs were compared, it was determined that the cost of port catheter placed by interventional radiologist was lower. However, it has been concluded that placement of ports in a special reserved environment by general surgeons and/or interventional radiologists instead of academic centers can reduce costs by minimizing overheads [14].

How is port catheter placement performed under ultrasound guidance?

In clinical practice, while inserting an ultrasound-guided port catheter;

I-The anatomy of the insertion site and the localization of the vessel should be determined,

II- It should be checked whether the vein is open,

III-Ultrasound should be used as a guide for venous puncture,

IV- The position of the needle in the vein should be checked,

V-Catheter position in vein should be checked [15-17].

What are the port catheter complications?

Port catheter complications can be evaluated as early if they occur within 30 days of implantation, and as late complications if they occur after 30 days. Early complications are intravenous or cardiac malposition, arrhythmias, hemothorax and cardiac tamponade as a result of perforation and bleeding, pneumothorax, ductus thoracic injury and air embolism. The universal use of ultrasound guidance for vein puncture has significantly reduced procedural and early complications [18]. Late complications include infections, venous thrombosis, pulmonary embolism, catheter breakage, migration and air embolism [19, 20].

Complications can be minor or major. Minor complications are those that do not require surgical or medical treatment within more than

24 hours. Major complications are those that require surgical or medical intervention in less than 24 hours, require hospitalization, and can lead to consequences, even to death. Hemothorax and pneumothorax are the most common major complications [18, 19].

In a study, complications were found in 34 (4%) patients out of 827 patients who underwent port catheterization between 2013 and 2015. As complications of chamber insertion, infection was seen in 5 patients (0.6%) and erosion in 6 patients (0.7%). The most common complication was catheter-related complications (n=19, 2.3%). It was found that catheter-related infection was seen in 7 patients (0.8%), catheter migration in 8 patients (1%), catheter-related thrombosis in 4 patients (0.5%), and chamber malposition in 2 patients (0.3%) [21].

In another study, in which 782 patients were evaluated between 2010 and 2018 to evaluate the early and late complications of port catheters, the most serious complication was pneumothorax in 7 patients and thrombotic occlusion of the catheter as a late complication. 2/3 of patients with thrombosis-related obstruction required thrombolytic treatment [22].

In a study of 399 patients who underwent chemotherapy between 2013 and 2017, the complication rates of port catheters or peripheral inserted central catheters were evaluated (peripheral inserted central catheter n=201 and port catheter n=198). 16 (8%) deep venous thrombosis was found in the peripheral inserted central catheter group, while 2 (1%) patients had port catheter group [23].

The patients were examined for port-related complications and thrombosis including port occlusion. Routinely, catheter care was done by using of heparin. In a study on this subject, there was no difference between the common and rare port care groups in terms of serious port-related complications during follow-up. However, the rate of thrombosis was found to be slightly higher in the rare port care group [24].

What is the effect of the port catheter on the patients' quality of life?

In a study evaluating the effects of peripheral venous catheters and central port catheters on the quality of life of patients with breast cancer and colon cancer; Complication rates of these two catheters were found to be similar. However, although port catheter procedures are slightly more painful than the other procedures, it has been found to have more positive results on quality of life when examined from a psychosocial perspective [25]. It has been found that port catheters have positive effects on the quality of life of patients with breast cancer, even if they are placed in different regions (chest, arm, trapezius muscle, etc.) in patients with breast cancer [26, 27].

Conclusion

These catheters, which can be placed safely and easily in patients with chronic diseases requiring recurrent venous intervention, have an important place in blood analysis and treatment without impairing the quality of life of the patients.

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Journal of Bionic Memory **Review article**

Deep brain stimulation for psychiatric disorders: A review

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ABSTRACT

Deep Brain Stimulation (DBS) is a neurosurgical procedure via the placement of neurostimulator, which is a medical device also known as brain pacemaker. The electrical impulses, which are sent to s pecific targets of brain through implanted electrodes, used in the treatment of some neurological and psychiatric disorders. While the mechanisms of action of DBS on the physiology on brain cells and neurotransmitters are controversial, it is well known that high-frequency electrical impulses into specific brain areas can diminish certain symptoms of some neurological and psychiatric disorders. DBS is already approved as a treatment for several neurological disorders by the Food and Drug Administration (FDA). It is approved as a treatment for essential tremor in 1997 and Parkinson's disease since 2002, for dystonia in 2003 and for epilepsy in 2018. There are also variety uses of DBS in psychiatric disorders with resistance to treatment, such as obsessive compulsive disorder, Tourette's syndrome, major depressive disorder, post-traumatic stress disorder, appetite disorders, alcohol and substance use disorders and also schizophrenia. This article outlines using of deep brain stimulation as a treatment method for psychiatric disorders which are resistant to medical treatments and psychotherapies, as well as the appropriate anatomical targets and the possible mechanism of actions.

Key words: Deep brain stimulation (DBS), psychiatric disorders, resistant, treatment.

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Introduction

The development of modern deep brain stimulation (DBS) begins with the investigations of the treatment choices for Parkinson's disease, in late 1980s [1]The discovery of the beneficial effects of electrical stimulation to basal nuclei on the improvement of the Parkinson's disease symptoms can be accepted as landmark for DBS application areas. Subsequently, some other neurological diseases including dystonia, essential tremor, and epilepsy were begun to treat via DBS. In the course of time, DBS has also been begun to treat psychiatric disorders with resistance to psychopharmacology and psychotherapy. Obsessive and compulsive disorder is the first psychiatric indication for DBS, approved by FDA. Clinical outcomes of psychiatric improvement following DBS in obsessive-compulsive disorder (OCD) and the developments in neuroimaging studies opened up new frontiers for other resistant psychiatric diseases. In the length of time, uses of DBS have begun to include other psychiatric disorders, such as Tourette's syndrome, major depressive disorder, post-traumatic stress disorder, appetite disorders, alcohol and substance use disorders and schizophrenia.

While the exact mechanism of action of DBS is not well known yet, there are some hypotheses

which try to explain the mechanisms [2,3,4,5]. One of the most considered hypotheses is the blockade of the depolarization and consequently blockage of neuronal output by direct effect of electrical currents. The other hypothesis is the synaptic inhibition of the neurons which are near the stimulating neurons, via the activation of inhibitory axon terminals with synaptic connections to neurons near the stimulating electrode. There is another hypothesis about desynchronization of abnormal oscillations of neurons near to the electrodes. Antidromic activation of the neurons near the electrodes is also a considered hypothesis.

DBS is a non-destructive procedure and this provides significant benefits such as being adjustable and largely reversible [6]. However, since it is a neurosurgical procedure, it may lead to some postoperative complications. Intracerebral hemorrhage is one of the most significant early postoperative complications and the risk is approximately 1%-%3 per lead [7]. Central nervous system infection is another significant early postoperative complication and the risk is around 1%-9% [8].

Ischemic stroke (1%), seizure (0-3%), and postoperative confusion (21%) are other possible complications [9]. Since DBS is an invasive surgical procedure and it can lead to such complications, it must be thought in psychiatric diseases for only resistant conditions. Therefore, DBS is thought as a treatment choice in psychiatry only when obsessive-compulsive disorder, Tourette's syndrome, major depressive disorder, post-traumatic stress disorder, appetite disorders, alcohol and substance use disorders and schizophrenia are severe, intractable and resistant to maximal psychotherapy and several psychotherapies.

Obsessive-Compulsive Disorder

Obsessive-Compulsive Disorder (OCD) is one of the most common psychiatric illnesses, affecting approximately 2–3% of the general population [10]. About 10% of the patients are accepted as treatment-refractory, since they have still intractable symptoms despite of proper pharmacological and psychotherapeutic treatments. [11] For some of these patients, deep brain stimulation offers an appropriate treatment choice and OCD is the first psychiatric indication for applying of DBS, approved by FDA in 2009 [12]. Therefore there are several case reports and trials about using of DBS to treat OCD. Clinical outcomes of psychiatric improvement following DBS in Obsessive-Compulsive Disorder (OCD) has opened up new frontiers for other treatment-resistant psychiatric diseases.

Since OCD is associated with the abnormalities of corticobasal nuclei networks, there are several targets of DBS for OCD [13]. Some targets are more effective since they have ability to capture prefrontal, anterior cingulate and basal nuclei connections of limbic system, including anterior limb of internal capsule (ALIC) which modulates anterior cingulate cortex (ACC) and orbitofrontal cortex (OFC) connections, medial subthalamic nucleus which modulates the OFC/ACC hyperdirect pathway and the subthalamic nucleus–ventral pallidal loop, ventral striatum which modulates reward system, and midbrain target which modulates the ascending ventral tegmental area fibers[13]. The studies demonstrated that there had been no significant difference in clinical outcomes between these targets [13,14].

In a meta-analysis study which was performed in 2015, thirty-one studies containing 116 subjects were addressed. For 83 subjects, DBS was applied to striatal areas, including anterior limb of the internal capsule, ventral capsule and

ventral striatum, nucleus accumbens and ventral caudate. For 27 subjects, DBS was applied to subthalamic nucleus. And for 6 subjects, DBS was applied to inferior thalamic peduncle. The findings of the study expressed that the reduction in global percentage of Yale-Brown Obsessive Compulsive Scale had been estimated at 45.1% and global percentage of responders at 60.0% [1].

In another prospective observational study, DBS was applied to bed nucleus of the stria terminalis/anterior limb of the internal capsule of six patients suffering from severe to extreme treatment resistant OCD. They were followed for four to eight years and the results demonstrated that four of six patients with treatment resistant OCD had shown a permanent improvement after DBS to ALIC [15].

Treatment Resistant Depression (TRD)

Despite of maximal medical and psychiatric therapy for long years, approximately 20% of depression patients continue to present symptoms [7]. For these group of patients, especially who still have had multiple episodes of major depression for long years with Hamilton Depression Rating Scale between 25-40 despite they were applied all other treatment choices including maximal pharmacotherapy and cognitive-behavioral therapy, DBS seems to be an effective choice [7] .There has been two beneficial guides to select the targets for DBS in Treatment Resistant Depression. One is clinical outcomes of psychiatric improvement following DBS in Obsessive-Compulsive Disorder, and the other one is neuroimaging studies [16,17]. The neuroimaging studies and both open-label and randomized controlled trials to date demonstrate that Subcallosaal Cingulate Cortex, Nucleus accumbens, Ventral Capsule and Ventral Stiratum and Medial Forebrain Bundle seemed to be main targets for DBS in treatment resistant depression. The most common investigations have been focused on Subcallosal Cingulate Cortex (SCC), also referred to as Brodmann area 25 (BA25) or subgenual cingulate (Cg25). It has multiple connections including nucleus accumbens, hypothalamus and brain stem. Activity increase in SCC has been thought to lead to depressive symptoms, and a decline in increased activity of this region has been linked to normalization of the activates of other brain regions which are connected to SCC, including nucleus accumbens, hypothalamus and brain stem. These connections of SCC allows for clinical response to DBS, including normalization of lack of interest, anhedonia, appetite problems, circadian and sleep disturbances, and abnormal stress responds and cortisol metabolism [18].One of the open label and single blind trials, which was performed by Holtzheimer et al. in 2012 with 17 participants, were reported with 65% response and 41% remission [7]. Another studied region of brain for DBS in TRD is nucleus accumbens, which has been demonstrated as smaller size and decreased activation to reward in severe anhedonia [19]. There are 11 open label case series, which was reported by Bewernick et al in 2012. They conducted 45% response and 9% remission one to two year follow up after DBS procedure [20]. Ventral Capsule/Ventral Striatum (VC/VS) is also an investigated area for DBS in TRD. Activity increase in VC/VS and its connections found positively correlated to higher depression scores in the CES-D score [21]. A randomized, double blind, sham-controlled, multisite study with 30 participants was published by Dougherty et al in 2014, with the result of 23% response and no significant difference between sham & control arms [22]. Another target for DBS in TRD is Medial Forebrain Bundle,

which plays a crucial role in the reward pathway. It has been pre-operatively showed that there was a strong linkage between the active electrode contact and the medial PreFrontal Cortex, by using individual Deterministic Diffusion Tensor Imaging [17]. In 2013, Schlaepfer et al published 7 case series. The results were 86% response and %57 remission rate on the background of 12 to 33 week follow up [23]. Another study about DBS in TRD was published by Fenoy et al. in 2016. The result of the study, which was an opel label trial with 4 participants, was 66% response on the background of 26 weeks [24]

Tourette syndrome (TS)

While there are more than 7 different targets for DBS as a treatment method for Tourette's syndrome (TS), it can be claimed that main targets which have essential roles for treatment of TS by DBS are the centromedian-parafascicular thalamic complex (CM-PF) and the Globus pallidus interna. There are plenty of studies which have been reported about successful treatment of TS with stimulation in the CM-PF and ventral tier of the thalamus [25]. About DBS of Globus pallidus interna to treat severe Tourette's syndrome, largest series reporting a mean decrease in Yale Global Tic Severity Score of 50% were published in 2012[26]. In a recent study which was performed with eight adult patients who were resistant to Tourette's syndrome medically, bilateral electrodes were implanted in the centromedian-parafascicular thalamic complex and the nucleus ventro-oralis internus. On the course of one following year after DBS to these areas of thalamus, it has been reported that tic severity symptoms and comorbidities were diminished and the quality of life improved [27].

Treatment Resistant Schizophrenia

Up to 30 % of Schizophrenia patients are thought to be the resistant to antipsychotic drug treatment, and 60% of these includes resistance to Clozapine [28]. Researchers investigated targeting the nucleus accumbens (NAc), hippocampus, globus pallidum internal segment, mediodorsal thalamus (MD), and medial septal nucleus (MSN) to be able to have a decline in the positive symptoms and improve the negative symptoms of schizophrenia patients with anti-psychotic resistance including Clozapine [29]. The most effective results seemed to be obtained in the studies which targets NAc by DBS. One of the cases is conducted by Corripio et al. NAc of schizophrenia patient was targeted by DBS and it was observed a 62% reduction in positive symptoms and 33% improvement in negative symptoms, following 4 weeks of unilateral left side stimulation[30]. There is also a pilot randomized cross-over clinical trial which investigated the effectiveness of DBS on eight schizophrenia patients with the resistance to anti-psychotic treatment including clozapine. Nucleus accumbens and subgenual anterior cingulate cortex regions of their brains were targeted by DBS. This tiral demonstrated that the placement of the electrodes in nucleus accumbens had more effective results than that in the subgenual anterior cingulate gyrus. Moreover, according to this trial, targeting of nucleus accumbens by DBS seemed to be beneficial on hallucinations and delusions [28].

Post-Traumatic Stress Disorder (PTSD)

The use of DBS to treat PTSD mainly aims to change the activity of the regions distant from the target, via the activation of the neuronal projections [31]. Glutamatergic projections from infralimbic neurons of ventromedial prefrontal cortex to intercalated cells of

amygdala play an essential role in the ceasing Central Amygdala cell activation, consequently leading to fear extinction [32]. Animal models showed that high frequency stimulation of the infralimbic neurons of ventromedial prefrontal cortex caused a decline on firing frequency of BasoLateral Amygdala principal cells, which is thought to be secondary to an increase in intercalated cell stimulation and inhibition of Central Amygdala cell activation [31,32]. A group of mice with poor fear extinction, which were closely similar to a clinical PTSD in humans, were used by .Reznikov et al. and study showed that high frequency stimulation had led to a decrease in fear responses and anxiety behavior, as well as prevented return of PTSD-like symptom [31,33]. There are also some human cases about the using of DBS for the treatment of PTSD. One of these cases is a 48-year old-man with a combat-related PTSD which is resistant to treatment. After his bilateral BasoLateral Amygdala had been applied DBS, he was observed for 8 months and it was reported that his symptoms had diminished 35% without a major adverse event [34].

Appetite Disorders

DBS seems to be an alternative treatment option for Refractory Obesity and Anorexia Nervosa (AN). Studies have demonstrated that central nervous system had had plenty of potential DBS targets for both disorders. The Lateral Hypothalamus, Ventro Medial Hypothalamus and Nucleus accumbens have all been shown to have elements of success as DBS targets in animal models of refractory obesity [35]. DBS targeting bilateral Lateral Hypothalamus was performed by Whiting et al, in order to treat refractory morbid obesity. There was no serious adverse effects; trend toward weight loss in 2/3 patients was found [36]. One of the largest trials about DBS treatment of AN was demonstrated by Lipsman et al. in 2017. DBS of the subcallosal cingulate gyri of 16 patients who had AN disease was performed and the trial showed that the patients had a significant improvement in BMI as well as other psychological result [37].

Alcohol and Substance Use Disorders

While the exact mechanisms of DBS on its clinical effects are unclear, DBS is thought to be able to modulate and manipulate neural circuits in reward pathways, consequently enable to change addictive behaviors [38]. Three alcohol use disorder cases were investigated for the effect of nucleus accumbens stimulation by DBS, and found a decrease in alcohol consumption as well as craving levels. After DBS stimulation, two of three participants remained abstinent, while the third reduced his alcohol consumption considerably, at 1 year follow-up [39]. There are also two studies investigating the use of DBS on cigarette smoking and nicotine-dependence targeting the nucleus accumbens. One is conducted by Kuhn et al, which demonstrated 3/10 patients cessated smoking on the first attempt after surgery, without a relapse for a mean of 28 months conducted a study in nicotine craving and cigarette consumption. Moreover, the remaining seven participants had a significant decrease in cravings and consumption [40]. The other study, which was conducted by Mantione et al, demonstrated that nicotine craving and cigarette consumption had significantly decreased in a participant, who originally treated by DBS for refractory Obsessive-Compulsive Disorder[41].. A longitudinal, crossover case study with a 36-year-old cocaine-dependent male participant showed that craving and consumption of cocaine had

been decreased by active DBS targeting to nucleus accumbens [42]. There are also some case reports which demonstrated that DBS might be a treatment option for Methamphetamine addiction patients [43]. It can be claimed that there are more conducted studies about the effect of active DBS on heroin consumption or craving in heroin-dependent participants, than the other substance use disorder studies. Common results of these studies showed that targeting the nucleus accumbens had demonstrated a significant decrease in cravings and consumption, as well as increase in abstinent participants [44].

Conclusion

Psychiatric disorders can resist despite of psychopharmacology and psychotherapy and therefore seem to be one of the major sources of disability in the world. For the psychiatric disorders which are resistant to non-surgical treatment methods, DBS appears a promising treatment model. Up to date, the most common case reports and trials performing uses of DBS in psychiatric disorders have been conducted about refractory OCD, since it had been the first FDA approved disorder in psychiatry for DBS treatment. It can be accepted as the landmark of using DBS in psychiatry, because several outcomes have been provided from these and they have opened up new frontiers for other treatment-resistant psychiatric diseases. Developments in neuroimaging studies have also helped for using areas of DBS in psychiatry. Intracranial targets detected via the help of the developments in neuroimaging and specific circuits which were crucial for psychiatric conditions could be modulated. While the exact mechanisms of DBS on its clinical effects and its most available anatomical targets for the certain psychiatric diseases are still unclear, there have been plenty of case reports and trials which demonstrate the beneficial effects of DBS in neuropsychiatric disorders. However, it can be still claimed that DBS was a new modality, especially compared to Parkinson disease, essential tremor, dystonia, epilepsy and psychiatric conditions other than OCD. Treatment resistant depressive disorder and Tourette's syndrome can be claimed as relatively more performed psychiatric conditions, although they are behind OCD. What DBS for schizophrenia, PTSD, alcohol and substance use disorders, appetite disorders and other potentially suitable psychiatric conditions need are more trials and more outcomes as well as new developments in neuroimaging which will be able to show the topography of brain and facilitate the placement of electrodes at effective stimulation sites.

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Cochlear implantation and electro-acoustic stimulation: Current status and developments

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ABSTRACT

The number of people with hearing loss constitutes approximately 6.5% of the world population. Hearing loss leads to alienation from social environments and deterioration in quality of life in adults. Children with hearing loss, on the other hand, have lower literacy and lower educational attainments. There are auditory prostheses, called cochlear implant (CI) devices, which are designed using a special speech coding strategy to convert acoustic information into electrical stimulation for patients with inadequate traditional hearing aids used for rehabilitation of hearing loss. These devices are surgically implanted and cause direct stimulation of primary afferent neurons in the inner ear. The auditory nerve is stimulated by the electrodes placed on the cochlea, and thus the auditory message can be sent up to the auditory cortex. With CI, increases in speaking, language and comprehension skills can be achieved.

Key words: Hearing loss, cochlear implant, cochlea, electro-acoustic stimulation.

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Introduction

The number of people with hearing loss constitutes approximately 6.5% of the world population [1]. The World Health Organization estimated this rate as 0.8% for high-income countries [2]. The level of hearing loss, which is characterized as a decrease in the meaning and perception of sounds, is determined by a pure tone audiogram. Hearing thresholds are measured in decibels (dB) and are classified as mild (25-40 dB), moderate (40 55 dB), moderate (55-70 dB), severe (70-90 dB), and severe (> 90 dB) hearing loss classified [3]. According to the World Health Organization, it has been stated that when hearing loss is> 40 dB in adults and> 30 dB in children, there will be loss of function in people [4]. Severe hearing loss, which may occur before the age of three, seriously affects language development negatively [5]. The literacy level and education level of children with severe hearing loss also decrease seriously [6, 7]. It negatively affects their quality of life, learning and development in terms of school activities and social interactions [8]. Hearing loss in adults is also associated with low income and associated economic difficulties and poor quality of life [9-11].

Conventional hearing aids are the primary tool for auditory rehabilitation in patients with sensorineural hearing loss (SNHL). Inadequate amplification with conventional hearing aids and limitations about with these aids such as acoustic feedback, spectral distortion,

nonlinear/harmonic distortion, external ear canal occlusion, lack of view/visibility, orientation, and social stigma of hearing aid use, have led to the development of implantable hearing aids [12].

Cochlear implants (CI) are auditory prostheses that convert acoustic information into electrical stimulation. Bipolar spiral ganglion neurons and primary afferent cells are used by CI without intermediary for electrical stimulation. CI follows a mechanism based on the principle of stimulation of the cochlea by means of electrodes placed up to the modiolus, and the direct stimulation of primary neurons by bypassing the electrical stimulation of the outer ear, middle ear and hair cells [12]. In short, electrical impulses bypass dysfunctional hair cells and directly depolarize primary afferent neurons [12].

Historical development of devices, devices and the principle of operation of devices

The first documented electrical stimulation of the auditory system occurred in 1790 [13, 14]. In addition, alternating currents, various charges, polarities and densities have been tried in various studies [15, 16]. In 1930, it was shown that electrical signals coming from the cat cochlea and very similar to waveforms can be copied and generated [16, 17].

An electrode combined with a receiver coil was implanted in a patient who had a distal cochlear nerve resection in 1957, and it was shown that the device could be stimulated with an external coil for several months. This stimulation enabled the patient to recognize sound awareness and simple words [14]. At the beginning of the 1960s, experiments were started by placing simple wires, wires with ball electrodes, and even simple strings in the scale tympani [15, 18]. In the light of these studies, implantable hearing aids began to be developed in 1972. In this way, the first clinical trials were started in 1973 [13, 18]. The validity of direct electrical stimulation of auditory nerve fibers (electroacoustic stimulation) as a rehabilitation strategy was accepted in 1977 [14, 19]. After single-channel implanted devices, multi-channel CI devices with open-set word recognition started to be developed [14, 20, 21]. Today, there are various devices produced by three different companies (Cochlear Corporation, Med-El, Advanced Bionics) with different electrode numbers and lengths [12, 22].

All CI systems consist of two main parts, an outer part containing a microphone, sound processor and transmission system, and an inner part containing the receiver/stimulator and electrode array. Generally, an external microphone picks up ambient sound and speech and sends the information to a body-worn or ear-level type sound processor. The speech processor converts the sounds into electrical signals sent over the skin or to the internal receiver/stimulus via radio frequency transmission. Transmission of the signal occurs when the external magnet in the transmitter is successfully aligned with the internal magnet in the receiver/stimulator. The receiver/exciter part decodes the signals and transmits them to electrodes located in the cochlea. Nerve stimulation occurs thanks to the electrodes and this stimulation is transmitted to the auditory center in the cortex [12].

Patient selection

In addition to a complete physical examination, a detailed otolaryngology and head and neck examination should be performed. However, the first step in patient selection is an audiological evaluation, and the level of hearing loss must be evaluated. After the evaluation of candidates for CI, imaging

methods (computed tomography and magnetic resonance imaging) should definitely be used [22].

When the adult selection criteria in the latest clinical studies for cochlear implantation are evaluated, firstly, a pure tone average (PTA) hearing level of 70 dB or higher, secondly, at least three months of appropriate hearing aid use or adequate amplification, and thirdly, discrimination scores, namely speech comprehension scores are less than 50%, fourthly, the central auditory pathways and cochlear nerve are complete in the evaluations, and finally, there are no contraindications to surgery [12].

Comprehensive audiometric assessment with air and bone conduction thresholds between 250 and 8000 Hz, along with speech discrimination scores, is essential for initial assessments [22].

Considering the candidate evaluation criteria for CI in the childhood age group; It can be done in any age group from 12 months to 17 years old. Deep SNHL (PTA thresholds ≥90 dB HL); is the absence of developmentally appropriate auditory capacity, defined as 20% to less than 30% on monosyllabic word tests, with minimal benefit from hearing aids and measured using parent-reported scales for younger children. Other criteria are defined as the completeness of the central auditory pathways and the cochlear nerve and the absence of any contraindication to surgery. In addition, having a hearing aid for at least 3 to 6 months before CI surgery, realistic expectations of family members, and enrollment in a postoperative rehabilitation program that supports the development of auditory skills are also important criteria [12].

It is difficult to determine the degree of hearing loss in infants and children with PTA evaluation. Also, applying speech audiometry is not easy in these age groups. For this reason, behavioral audiometry is more prominent for evaluation purposes in these age groups. Initial hearing loss must be confirmed by auditory brainstem responses (ABR) and otoacoustic emission (OAE) [22, 23].

Language and intelligence assessments are also important, especially in the pediatric population, as the ultimate goal of cochlear implantation is effective communication. A psychological assessment is performed to assess the child's verbal and nonverbal intelligence, attention and memory skills, and visual-motor integration. It is also important to know the cognitive abilities of the child when considering a child for CI, pre-counseling the family and planning possible rehabilitation needs later [24].

Bilateral cochlear implantation applications

In the pediatric age group, unilateral CI practice provides significant benefits for speech recognition in a quiet environment and meets a person's basic auditory needs. However, in patients with bilateral hearing loss who underwent unilateral CI, difficulties may be experienced in ambient noise and multiple sound environments. More difficulties may be seen in perceiving the direction of the sound [25]. Hearing with two ears is always much more effective than hearing with one ear, considering the shadow effect of the head, the gathering effect of binaural sound, and the effect of silencing binaural noise [26, 27]. The ability to form new neural connections in the brain is greatest in the first 3.5 years [28]. Therefore, it is critical for auditory development and language acquisition in the early stages of life [28]. Early CI in early detected hearing loss may prevent permanent changes in the auditory cortex [29]. While unilateral CI contributes to the development of

the auditory pathways and auditory cortex on the operated side, maturation cannot occur on the non-implanted side [28, 30]. Another issue is that, unlike sequential bilateral CI at different times, simultaneous bilateral CI is more effective and it should be known that the gains can be higher [31].

Bilateral CI is also significantly beneficial in the adult age group [25]. Bilateral CI applications are more beneficial in people with meningitis, acute bilateral profound hearing loss, and vision problems in addition to hearing loss. Bilateral CI may improve the auditory function of these patients. However, bilateral CI applications are applied less frequently in the adult age group than in the pediatric age group [28].

The group that can benefit more from bilateral CI in the adult age group and is applied more is the young adult group. Significant auditory support and improved sound localization for better hearing in noisy environments in these age groups can provide significant advantages for education and employment opportunities [29].

Gains after cochlear implant surgery

In the postoperative period, patients in the adult age group have a more advanced voice perception ability compared to the preoperative period. This perception is particularly pronounced at higher frequencies. Sound detection thresholds are approximately 25 to 30 dB HL in the range of 250 to 4000 Hz postoperatively [32]. Adult patients who develop post-lingual hearing loss after language development generally have a significant increase in speech perception levels after the first month postoperatively. In patients with pre-lingual hearing loss before language development is completed, the gains are lower compared to the post-lingual group. However, even pre-lingually, there can be significant improvements in speech perception after CI [12].

Auditory gains of approximately 25 dB HL for frequencies of 250 to 4000 Hz for adults in the postoperative period are also valid for the pediatric age group. These levels are important for the development of auditory skills and communication. Studies with children show that earlier CI is necessary for high performance [12]. It should also be known that postoperative performance and speech-perception skills are adversely affected in patients with a short period of hearing aid use before CI [12]. It is also known that there is a steady increase in language and speech performance for 3 to 5 years in the postoperative period. Determination of suitable candidates before the surgery and the rehabilitation program applied after the surgery have a great impact on the success of cochlear implantation. Different evaluation and follow-up processes are applied in pre-lingual and post-lingual patients [12, 33].

Conclusion

Cochlear implantation, in which the auditory nerve is directly stimulated by means of electrodes placed in the cochlea, is a significantly useful method for the development of hearing skills and the emergence of a language and speech close to normal in patients with severe hearing loss.

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