

Original Article

Preliminary application of hybrid operation in the treatment of carotid artery stenosis in patients with complex ischemic cerebrovascular diseases

Liyong Zhang, Tao Xing, Fenyang Geng, Lixin Du, Jiyue Wang

Department of Neurosurgery, Liaocheng People's Hospital, Liaocheng 252000, Shandong, China

Received June 5, 2014; Accepted July 23, 2014; Epub July 15, 2014; Published August 1, 2014

Abstract: Along with the recent development of intraluminal interventional techniques and correlated imaging methods, one-stop hybrid operation has become a new focus in clinical settings. The aim of this study is to discuss the clinical significance of the one-stop hybrid endarterectomy surgery in the treatment of complex ischemic cerebrovascular diseases. In this study, clinical data from 10 patients with complex ischemic cerebrovascular diseases (including multi-vessel severe stenosis of the internal extracranial carotid artery, single vessel series stenosis of the internal extracranial carotid artery, in-stent restenosis, complete occlusion of the common carotid or the internal carotid artery) admitted to Beijing Xuanwu Hospital and Liaocheng Brain Hospital, were retrospectively analyzed. All enrolled subjects underwent three types of hybrid operations. The clinical efficacy of this surgery was subsequently assessed in this clinical trial. The results indicated that no related surgical complications were noted during the perioperative period. Intraoperative and postoperative imaging revealed no signs of vascular stenosis, the blood supply recovered, and clinical symptoms were alleviated. The follow-up lasted for 6 to 12 months. Imaging re-examination showed no evidence of re-stenosis and good blood circulation was present in the recanalized blood vessels. Favorable treatment efficacy was achieved. The intracranial blood supply was significantly improved postoperatively. In conclusion, one-stop hybrid operation plays an important role in treating complex stenosis cerebrovascular diseases.

Keywords: Carotid artery diseases, endarterectomy, carotid artery stenting, one-stop hybrid operation

Introduction

Along with the recent development of intraluminal interventional techniques and correlated imaging methods, one-stop hybrid operation has become a new focus in clinical settings [1, 2]. Intraluminal interventional technique is defined as an integrated technique that incorporates vascular intervention, surgery, and medical imaging, and is utilized for clinical diagnosis and treatment [3]. Due to the complexity of cerebrovascular diseases, integrative therapies that involve vascular intervention and traditional surgery are urgently required. In this study, one-stop hybrid operation was employed to treat 10 cases with complex cerebrovascular diseases, and we are presenting the clinical outcomes below.

Materials and methods

Study subjects

A total of 10 subjects diagnosed with complex ischemic cerebrovascular diseases (including multivessel severe stenosis of the extracranial internal carotid artery, single vessel extracranial series stenosis, in-stent re-stenosis, and complete occlusion of the common or carotid arteries) between March 2010 and December 2013 were enrolled in this clinical trial. Six participants were admitted to Xuanwu Hospital of Capital Medical University and 4 to the Liaocheng Brain Hospital. Six patients were males and 4 were females, aged 63 ± 14 years on average. Seven patients showed refractory episodes of unilateral limb weakness and

Hybrid operation for carotid artery stenosis

numbness, 4 had intermittent dizziness, and 3 had been hospitalized due to cerebral infarction of the affected side. Two cases showed unilateral hemiplegia before admission, 5 had a history of smoking, 6 had hypertension, and 4 suffered from diabetes.

Inclusive and exclusive criteria

Inclusion criteria: the temporary onset of cerebral ischemia in the carotid/vertebral artery system (TIA); carotid artery imaging showing severe stenosis of the carotid/vertebral artery, exceeding 50% of the vessel diameter or the inner diameter of residual vessel < 2 mm; re-stenosis following carotid artery stenting; pathological changes of series stenosis at the distal end of carotid artery; carotid artery stenosis located under the clavicle, with a high degree of bifurcation or pathological changes above C2.

Exclusion criteria: During the acute phase of cerebral infarction caused by carotid artery occlusion, vascular reconstruction probably aggravates hydrocephalus and is likely to make ischemic cerebral infarction degenerate into hemorrhagic cerebral infarction. Exclusion criteria were: neck related factors, such as radiotherapy on the same side of neck, or vocal cords paralysis on the opposite side and the patient underwent tracheotomy; serious systematic diseases, with the inability to undergo surgery, such as severe cardiopulmonary diseases, malignant tumors, and patients unable to survive surgery; complications caused by alternative diseases; requirement for open heart surgery within 6 weeks; fluctuating angina; having had a heart infarction during the previous 6 months; congestive heart failure and difficult to control hypertension; and diabetes.

Lesions types

Two cases had serious stenosis of the carotid artery unilaterally, complicated with severe stenosis at the opening of the same side common carotid artery, and 3 patients presented with re-stenosis after carotid artery stenting. One patient was unable to undergo femoral artery puncture due to other reasons and was complicated with carotid artery series stenosis. Two cases failed to undergo conventional surgery due to high bifurcation of carotid artery or the relatively high position of carotid artery atherosclerotic plaque, and two additional partici-

pants presented complete occlusion of the common and carotid arteries.

Surgical approach

The operating room should be equipped with a variety of equipments required to perform the hybrid operation, such as an X-ray angiography system in a constrained room, real-time ultrasound, anesthesia machine, surgery appliances, and a laminar flow system. All the equipments should be properly coordinated.

Ten patients received one-stop hybrid operation (simultaneous delivery of surgery and interventional therapy). There were three types of operations: ① Endarterectomy plus stenting on the affected side. ② Stenting of the carotid artery under direct vision. ③ Catheter endarterectomy plus Foley's tube embolectomy under perspective view.

Postoperative treatments, such as the use of anti-platelet drugs (dosage and usage) and checking whether the blood pressure was controlled, were conducted. All patients were transferred to the intensive care unit in the Department of Neurology (NICU). Measures including persistent cardiac electric monitoring and persistent low flow oxygen therapy were conducted. Proper analgesic treatment was delivered to avoid excessive irritation. The neck wounds were cooled by compression with an ice bag. The activated coagulation time (ACT) was monitored and heparin sodium was administered by intermittent subcutaneous injection or via a persistent pump. ACT was maintained between 180 and 200 sec. Mannitol (125 mL, q8h) and dexamethasone (10 mg) were given on the day of surgery and 3-5 d postoperatively. Intravenous administration of calcium ion antagonists was performed in patients with hypertension as necessary, to control the blood pressure and the heart rate. The systolic pressure of the injured artery was maintained between 110 and 150 mmHg (1 mmHg=0.133 kPa). Those complicated with coronary heart diseases were persistently be administered nitric acid and glycerol simultaneously, via a pump, to improve the coronary blood supply. The electrolyte and acid-alkali imbalance was rectified based on the outcomes of the blood gas analysis. Routine blood tests, liver and renal functions, changes in the myocardial enzymes, dynamic electrocardiogram changes,

Hybrid operation for carotid artery stenosis

Table 1. Clinical outcomes of one-stop hybrid operation

Outcome	Significant improvement			No remission
	Completed remission	Satisfy outcome	Better outcome	
Cases (n)	5	3	1	1
Percentage (%)	50%	30%	10%	10%
		90%		10%

Table 2. Side effects of one-stop hybrid operation in subjects

Side effects	Cases (n)	Percentage (%)
Wound swelling	2	20%
Easily irritable, intermittent headache, poor sleep	4	40%
Coughing and hoarseness	2	20%
Transient high blood pressure	1	10%
Amaurosis	1	10%

postoperative neck hemorrhage, limb mobility, and muscle strength were regularly examined and monitored. Relevant tests and effective treatments were immediately conducted for patients presenting hemorrhage and hematoma in neck wounds, and in those with abnormal mental status and abnormal physical signs of nerve localization. Surgical hemostasis was performed as necessary.

Results

Clinical outcomes

Postoperative examinations (intraoperative DSA, TCD and postoperative vascular ultrasound, CTA and DSA) and 2 years follow-up in all patients revealed that the intracranial blood supply was significantly improved (**Table 1**). No severe surgical complications were observed. One case showed no significant changes compared with preoperative status. Five patients' symptoms were fully alleviated. The muscle strength on the affected side was strengthened postoperatively and achieve satisfactory outcome in 3 subjects. One subject received better outcome. From the above results, we found that 90% subjects' symptoms were significantly improved. What's most important is that 80% subjects received the satisfy outcome, and only 10 received no remission.

Side effects

Though the one-stop hybrid operation received very satisfied outcomes, a few side effects

were also discovered (**Table 2**). One case had amaurosis after surgery and the symptoms of intermittent dizziness were significantly alleviated. Two cases showed signs of wound swelling, which was allayed after receiving effective treatments, such as spectrum radiation and swelling-reducing therapy. Four patients became easily irritable, had intermittent headache, poor sleep, and a slight degree of excitement. These symptoms were gradually allayed after effective therapy, such as moderate sedation for 3

to 5 d. Two patients presented post-surgery coughing and hoarseness, and in two patients these improved after symptomatic therapy, whereas one patient had hoarseness and was followed up. One patient presenting transient high blood pressure and poor control received symptomatic therapy.

One-stop hybrid operation improves stenosis in beginning segment of left arteria carotis communis and internal carotid arteries

A male patient, 65-year-old, was admitted to Liaocheng Brain Hospital in July 2011 due to "intermittent dizziness, transient amaurosis for 2 years that were aggravated for half a year". Upon admission, neck CTA examination showed severe stenosis in the beginning section of the left arteria carotis communis (**Figure 1A**) and carotid arteries and right carotid artery occlusion (**Figure 1B**). To treat common and carotid artery stenosis simultaneously, one-stop hybrid operation of endarterectomy and carotid artery stenting was employed. General anaesthesia was conducted via tracheal intubation, with the head tilted towards the right by 45°. An approximately 8 cm incision was made at the frontal edge of the left sternocleidomastoid muscle, skin and platysma were cut open, the frontal edge of sternocleidomastoid muscle was displaced, the carotid sheath was exposed and opened, and the carotid artery and its branches and the internal carotid artery were separated and exposed (**Figure 2A**). A retrograde puncture of the left common carotid artery was successfully conducted and a 6F artery sheath

Hybrid operation for carotid artery stenosis



Figure 1. Stenosis disappears in beginning segment of left arteria carotis communis and internal carotid arteries by head and neck CTA examination. A. The preoperative condition of the stenosis of left arteria carotis communis; B. The preoperative condition of the stenosis of left internal carotid arteries; C. The post-operative condition of the stenosis of left arteria carotis communis; D. The post-operative condition of the stenosis of left internal carotid arteries.

tube was retrograde-inserted into the left common carotid artery guided by a lead wire (**Figure 2B**). Then a Protege 9-25 balloon stent (PROTeGe, EV3, USA) was placed at the stenosis segment of the left common carotid artery opening. The stenting release was satisfactory. At 7 days postoperatively, skull and neck CTA showed that the signs of stenosis in the beginning segment of the left arteria carotis communis (**Figure 1C**) and internal carotid arteries (**Figure 1D**) disappeared.

One-stop hybrid operation triggers stenosis disappeared by digital subtraction angiography

Previous DSA tests showed high bifurcation of the carotid artery, extending to the lower margin of C2 (**Figure 3A**). In the hybrid operating room, the bifurcation of the carotid artery was exposed by conventional CEA surgery and it was found that the upper segment was not sufficiently exposed, making it impossible to com-

plete the operation. The patient presented with poor compensation of the intracranial blood supply (**Figure 3A**). The arterial blood circulation almost dropped to zero on the same side of the brain after attempts to occlude the common carotid artery. Carotid artery stenting under direct vision 9×60 mm (EV3 Covidien, USA) and carotid artery puncture under direct vision were adopted. The stenosis segment of the internal carotid artery was identified, carotid artery stenting was performed, hemostasis was delivered to the injured vessels, and the incisions were closed layer by layer. Post the operation, the stenosis was eliminated by stenting insertion (**Figure 3B**).

Vascular pulsatility index and blood circulation are improved significantly

Transcranial Doppler (TCD) monitoring for the cerebral arteries on the same side before and post operation was performed at 7 days post-

Hybrid operation for carotid artery stenosis

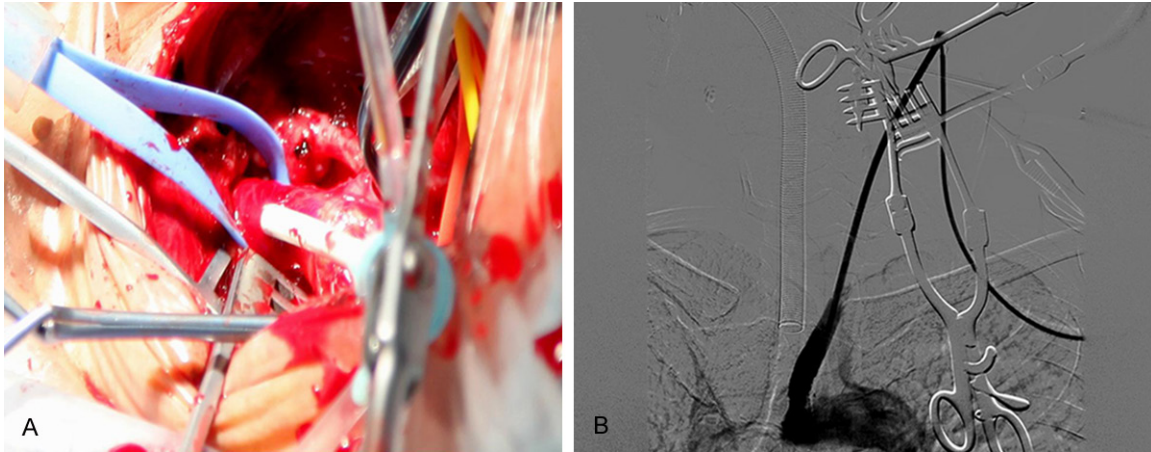


Figure 2. Operation process of One-stop hybrid operation. A. Retrograde puncture and intubation from the common carotid artery intraoperatively as observed under the microscope; B. Stent insertion into the beginning segment of the common carotid artery.

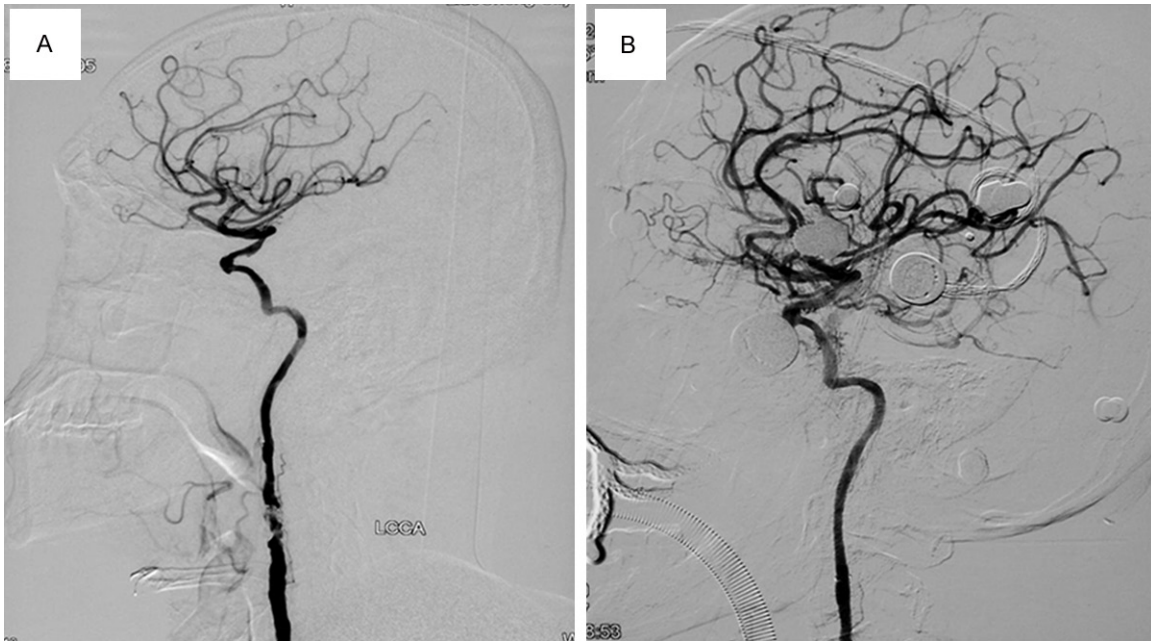


Figure 3. The stenosis changes following stenting insertion. A. The stenosis status at the time of preoperation; B. The absence of stenosis following stenting insertion.

operatively. The results indicated that skull and neck color ultrasound and TCD revealed that the blood circulation recovered well compared with pre-operation (Figure 4).

Discussion

Over 10 years ago, the concept of “hybrid operation” has been proposed, and it was initially applied in the surgical treatment of heart disease [4, 5]. At first, it was mainly utilized as a

staging treatment or postoperative intervention [6, 7]. Ischemic cerebrovascular diseases account for a large proportion of vascular and neurosurgical diseases. Most of these cases are affected by stenosis of the extracranial arteries that supply blood. Traditional surgical and vascular treatments are mainly employed. Traditional surgical therapy refers to endarterectomy (CEA), which has been applied for centuries and the latter is carotid artery stenting (CAS) [8]. These treatments have specific char-

Hybrid operation for carotid artery stenosis

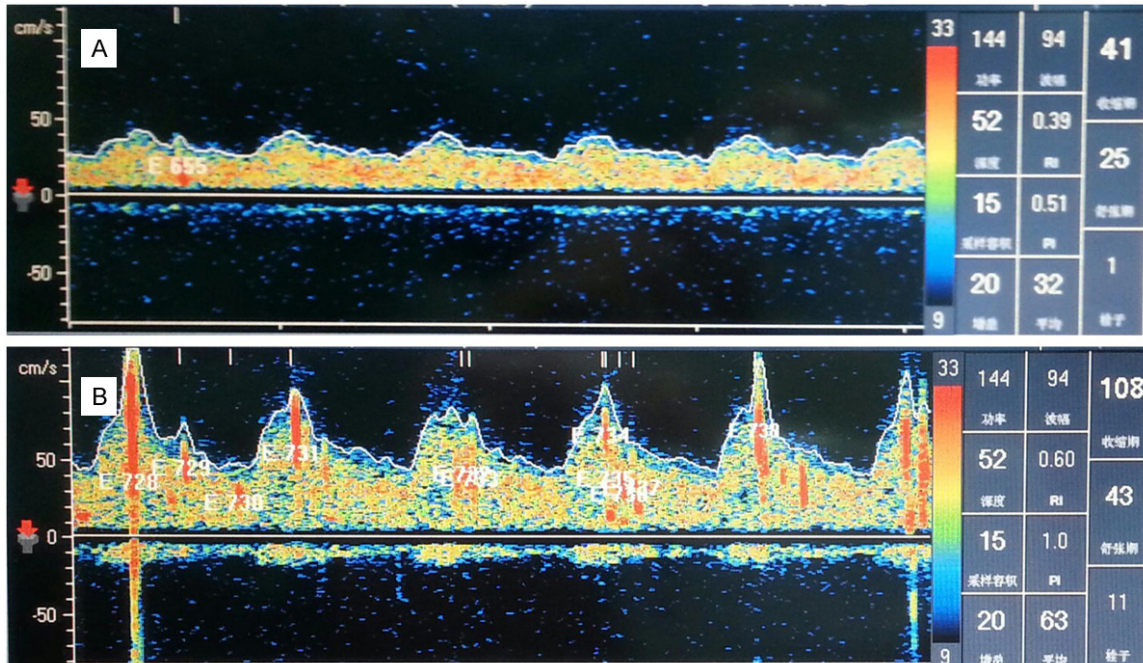


Figure 4. TCD monitoring data for the cerebral arteries on the same side. A. TCD monitoring data preoperatively; B. TCD monitoring data postoperatively.

acteristics and they complement each other. CEA is limited by poor tolerance towards surgery, high bifurcation of the carotid artery, and plaques extending beyond the surgically exposed area. CAS is constrained by severe tortuosity of the affected arteries, seriously calcified plaques, and chronic carotid artery occlusion [9, 10]. For complex vascular diseases, traditional surgery or vascular interventional therapy fails to obtain relative high efficacy. Hybrid operation becomes an alternative when CEA or CAS alone is not sufficient to treat refractory vessel lesions.

Judging from our clinical experience, one-stop hybrid operation is of clinical significance in breaking the boundaries between traditional surgery and internal vascular therapy. A hybrid operating room integrates the catheter intervention room, the anesthesia department, and the operating room, with high safety and sterile standards. The hybrid operation serves as a comprehensive platform to offer surgical treatment, interventional therapy, and imaging examinations, while maximizing clinical benefits [11], which reduces the times of transport and decreases the risk of adverse events induced by anesthesia, providing a novel treatment solution for ischemic cerebrovascular dis-

eases. More importantly, it can offer real-time evaluation of surgical efficacy, provide guidance for the smooth ongoing operation, save resources and costs and maximizes clinical efficacy, which is regarded as a new treatment mode in clinical settings.

The modes and procedures of hybrid operation are not fixed, whereas the other two techniques have default procedures and modes, which requires surgeons to be highly proficient at these operations. For these three types of surgeries, we have accumulated clinical experience that enabled us to perform surgery with an approximately 0.6% incidence for stenosis at the beginning section of the common carotid artery on the same side complicated with bifurcation branches of carotid artery [12]. It is difficult to verify which site of lesions leads to intracranial ischemic pathological changes on the same side. Therefore, the lesions at both sites should be treated simultaneously [13]. Karrothano et al [14] suggested that hybrid operation is more efficacious in addressing these lesions compared with surgical therapy alone and stenting treatment. ① Intraoperatively, retrograde placement of stenting at the beginning section of the common carotid artery should be conducted first to restore the blood supply of

Hybrid operation for carotid artery stenosis

common carotid artery. Thus, if insufficient compensation of the intracranial blood supply is caused by vascular blockage during endarterectomy, shunting may be utilized to guarantee brain perfusion intraoperatively. ② During common carotid artery puncture and retrograde placement of stenting, the internal carotid artery should be clipped to prevent the plaque from falling into the cranium. ③ When retrograde puncture of common carotid artery entering into artery sheath and stenting occurs, the operation should be performed under perspective view to prevent stenting, lead wire and artery sheath from causing the plaque to fall, and especially to prevent fatal aortic arch dissection caused by damaging the aortic arch intima [15].

Previous studies proposed repeated carotid artery stenting for patients with in-stent restenosis. However, this procedure fails to obtain desirable outcomes of vascular reconstruction or to fully restore blood vessels to their anatomical structures. Prior to formal beginning the operation, a variety of surgical plans have been proposed. ① The use of 9-60 mm stent in length. It is difficult to succeed by separating the stent alone due to high position of the upper end. If the stent was not completely separated, the stent at the site of stenosis will be cut and a new stent will be used to cover the cutting end of the original stent after vascular anastomosis. ② After stenting, peripheral vascular adhesion may be induced or hard plaque puncture wounds may be caused by balloon expansion for the first time. Artificial blood vessels should be prepared preoperatively to repair the defects of the outer membrane after stenting separation. ③ Common carotid artery puncture under direct vision and carotid artery stenting should be performed instead if the stent separation was not permitted intraoperatively. Only the upper margin of the stent can be exposed during dissection. Vascular blockage can be performed while it is impossible to place a shunt. Considering the poor health of patients, the third surgical scheme was employed to reduce the risks of this procedure. For these cases of in-stent restenosis surgery, multiple surgical plans should be prepared. Based upon intraoperative situations, vascular reconstruction and blood supply recovery should be performed as possible without threatening patients' lives [16, 17].

The following experience was summarized for patients with complete carotid artery occlu-

sion. ① Recanalization surgery with Fogarty balloon catheter may be considered for cases with complete occlusion of the internal carotid artery, when the occlusion segment does not exceed the ophthalmic artery. In general, the success rate of vascular recanalization for thrombus carotid artery occlusion treated by balloon surgery is relatively high. However, it is difficult to recanalize the vascular solid occlusion caused by atherosclerosis. ② For patients with common carotid artery occlusion, it is viable to recanalize both thrombus occlusion and solid occlusion. Scholars have successfully recanalized the common carotid artery by performing carotid endarterectomy [13]. ③ The authors in this study suggest that recanalization of both the common and the internal carotid artery should be conducted under perspective view to prevent the Fogarty balloon from extending beyond the carotid syphon segment of the internal carotid artery, which could result in vascular rupture. It is also designed to avert the inner membrane peeler and the elevator exceeding the opening of the common carotid artery and entering into the aortic arch, eventually leading to its dissection. ④ Stent covering via interventional approach has a high efficacy in treating plaque stenosis at the opening of the common carotid artery and ruptured inner membrane at the terminus of the internal carotid artery, and prevent the plaque from falling into the blood vessel during vascular dissection [12].

To sum up, "one-stop hybrid operation" has the following advantages: 1. is the possibility to adjust surgical strategy during the operation and transit between interventional therapy and traditional surgery according to specific circumstances; 2. The possibility to save the time required to transfer patients between imaging department and operating room and thus reduce surgical risk; 3. the possibility to properly combine traditional open surgery and internal vascular therapy in the treatment of vascular lesions and maximizing clinical efficacy. However, hybrid operation is still in its initial stages and has many problems to be addressed. This technique remains to be further explored by future investigations.

Acknowledgements

This research was supported by the national five year science and technology support program (Project No. 2011BAI08B04).

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Jiyue Wang, Department of Neurosurgery, Liaocheng Brain Hospital, 45 Huashan Road, Liaocheng 252000, Shandong, China. E-mail: wangjiyuedoc@yeah.net

References

- [1] Zhang M, Fang WY, Qu XK, Yuan F, Wang WG, Fei J and Wang ZG. AMPK activity is down-regulated in endothelial cells of GHS-R (-/-) mice. *Int J Clin Exp Pathol* 2013; 6: 1770-1780.
- [2] Shen L, Hu S, Wang H, Xiong H, Zheng Z, Li L, Xu B, Yan H and Gao R. One-stop hybrid coronary revascularization versus coronary artery bypass grafting and percutaneous coronary intervention for the treatment of multivessel coronary artery disease: 3-years follow up results from a single institution. *J Am Coll Cardiol* 2013; 61: 2525-33.
- [3] Shin JH. Interventional management of tracheobronchial strictures. *World J Radiol* 2010; 2: 323-328.
- [4] Terada T. Cutaneous hybrid tumor composed of epidermat cyst and cystic pilomatricoma expression p53 and high Ki-67 labeling. *Int J Clin Exp Pathol* 2013; 6: 1187-1189.
- [5] Kozlov IA, Novozhilov VA, Rasputin AA, Syrkin NV, Podkamenev AV, Iurkov PS, Solov'ev AA and Radikevich OV. Hybrid surgery for the treatment of ovarian cysts in newborns. *Khirurgiia (Mosk)* 2013; 10: 40-45.
- [6] Secinti KD, Ozalp H, Attar A and Sargon MF. Nanoparticle silver ion coatings inhibit biofilm formation on titanium implants. *J Clin Neurosci* 2011; 18: 391-395.
- [7] Schranz D, Michel-Behnke I, Heyer R, Vogel M, Bauer J, Valeske K, Akinturk H and Jux C. Stent implantation of the arterial duct in newborns with a truly duct-dependent pulmonary circulation: a single-center experience with emphasis on aspects of the interventional technique. *J Interv Cardiol* 2010; 23: 581-588.
- [8] Brott TG, Hobson RW 2nd, Howard G, Roubin GS, Clark WM, Brooks W, Mackey A, Hill MD, Leimgruber PP, Sheffet AJ, Howard VJ, Moore WS, Voeks JH, Hopkins LN, Cutlip DE, Cohen DJ, Popms JJ, Ferguson RD, Cohen SN, Blackshear JL, Silver FL, Mohr JP, Lal BK, Meschia JF; CREST Investigators. Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N Engl J Med* 2010; 363: 11-23.
- [9] Matsuda Y, Terada T, Masuo O, Matsumoto H, Ohshima K, Tsumoto T and Tsuura M. The clinical results of transcervical carotid artery stenting and frequency chosen as the approach route of carotid artery stenting in 1067 consecutive cases. *Acta Neurochirurgica* 2013; 155: 1575-1581.
- [10] Thapar A, Jenkins IH, Mehta A and Davies AH. Diagnosis and management of carotid atherosclerosis. *BMJ* 2013; 346: 1485.
- [11] Levien LJ, Benn CA, Veller MG and Fritz VU. Retrograde balloon angioplasty of brachiocephalic or common carotid artery stenosis at the time of carotid endarterectomy. *Eur J Vasc Endovasc Surg* 1998; 15: 521-527.
- [12] Allie DE, Hebert CJ, Lirtzman MD, Wyatt CH, Khan MH, Khan MA, Fail PS, Chaisson GA, Keller VA, Vitrella DA, Allie SD, Allie AA, Mitran EV, Walker CM. Intraoperative innominate and common carotid intervention combined with carotid endarterectomy: A true endovascular surgical approach. *J Endovasc Ther* 2004; 11: 258-262.
- [13] Grego F, Frigatti S, Lepidi S, Bonvini S, Amista P and Deriu GP. Synchronous carotid endarterectomy and retrograde endovascular treatment of brachiocephalic or common carotid artery stenosis. *Eur J Vasc Endovasc Surg* 2003; 26: 392-395.
- [14] Karathanos C, Sfyroeras GS, Stamoulis K, Drakou A, Vretzakis G and Giannoukas AD. Hybrid procedures for the treatment of multifocal ipsilateral internal carotid and proximal common carotid or innominate artery lesions. *Vasa* 2011; 40: 241-245.
- [15] Bazan H, Sheahan M and Dardik A. Carotid endarterectomy with simultaneous retrograde common carotid artery stenting: Technical considerations. *Catheter Cardiovasc Interv* 2008; 72: 1003-1007.
- [16] Marcucci G, Accrocca F, Giordano A, Antonelli R, Gabrielli R and Siani A. Results of surgical repair of carotid in-stent restenosis. *Cardiovasc Surg (Torino)* 2012; 53: 707-714.
- [17] Wan SY, Hu YC, Zhan YQ, Qin DD and Ding Y. Hemocoagulase atrox reduces vascular modeling in rabbit carotid artery adventitia. *Int J Clin Exp Pathol* 2013; 6: 2386-2395.