ISSN 2219-2832 (online)

# World Journal of *Surgical Procedures*

*World J Surg Proced* 2014 March 28; 4(1): 1-22

Baishideng Publishing Group
www.wjgnet.com

WJSP World Journal of Surgical Procedures

A peer-reviewed, online, open-access journal of surgical procedures

# Editorial Board

2011-2015

The *World Journal of Surgical Procedures* Editorial Board consists of 276 members, representing a team of worldwide experts in surgical procedures. They are from 35 countries, including Australia (10), Austria (3), Belgium (1), Brazil (4), Canada (5), China (23), Egypt (2), France (1), Germany (10), Greece (9), Hungary (1), India (6), Iran (3), Ireland (1), Israel (6), Italy (29), Japan (34), Lebanon (1), Lithuania (1), Mexico (2), Netherlands (2), Nigeria (1), Norway (1), Pakistan (1), Poland (1), Romania (2), Saudi Arabia (1), Singapore (2), South Korea (7), Spain (11), Switzerland (5), Thailand (1), Turkey (7), United Kingdom (11), and United States (71).

**Hungary**

Péter Örs Horváth, *Pécs*

**India**

Nilakantan Ananthakrishnan, *Pondicherry*
Rakesh Kumar, *Haryana*
Suguna Lonchin, *Chennai*
Chinmay Kumar Panda, *Kolkata*
Muthukumaran Rangarajan, *Coimbatore*
Nihal Thomas, *Vellore*

**Iran**

Mehrdad Mohammadpour, *Tehran*
Seyed Reza Mousavi, *Tehran*
Mohammad Taher Rajabi, *Tehran*

**Ireland**

Desmond Winter, *Dublin*

**Israel**

Nimer Najib Assy, *Safed*
Haim Gutman, *Tikva*
Yoav Mintz, *Jerusalem*
Solly Mizrahi, *Beer sheva*
Nir Wasserberg, *Petach Tiqua*
Oded Zmora, *Tel Hashomer*

**Italy**

Ferdinando Agresta, *Fregona*
Franco Bassetto, *Padova*
Claudio Bassi, *Verona*
Gabrio Bassotti, *Perugia*
Francesco Boccardo, *Genoa*
Giuseppe Brisinda, *Rome*
Fausto Catena, *Bologna*
Luigi D'Ambra, *La Spezia*
Alessandro Franchini, *Florence*
Giuseppe Galloro, *Naples*
Massimo Gerosa, *Verona*
Francesco Greco, *Brescia*
Roberto Iezzi, *Rome*
Fabrizio Luca, *Milan*
Simone Mocellin, *Padova*
Boscolo-Rizzo Paolo, *Padua*
Giacomo Pata, *Brescia*
Marcello Picchio, *Latina*
Giuseppe Piccinni, *Bari*
Marco Raffaelli, *Rome*
Matteo Ravaioli, *Bologna*
Raffaele Russo, *Naples*
Vincenzo Russo, *Naples*
Pierpaolo Sileri, *Rome*
Luciano Solaini, *Ravenna*
Pietro Valdastri, *Pisa*
Luca Viganò, *Torino*
Luigi Zorcolo, *Cagliari*

**Japan**

Hiroki Akamatsu, *Osaka*
Mitsuhiro Asakuma, *Osaka*
Hideo Baba, *Kumamoto*
Akihiro Cho, *Chiba*
Shotaro Enomoto, *Wakayama*
Satoshi Hagiwara, *Yufu*
Yoshiki Hirooka, *Nagoya City*
Motohiro Imano, *Osaka*
Yasuhiro Ito, *Kobe*
Koichi Iwatsuki, *Osaka*
Kyousuke Kamada, *Asahikawa*
Hirotoshi Kobayashi, *Tokyo*
Makoto Kume, *Gifu*
Daisuke Morioka, *Yokohama*
Toshitaka Nagao, *Tokyo*
Nobuhiro Ohkohchi, *Tsukuba*
Kensaku Sanefuji, *Fukuoka*
Norio Shiraishi, *Oita*
Yasuhiko Sugawara, *Tokyo*
Nobumi Tagaya, *Koshigaya*
Sonshin Takao, *Kagoshima*
Hiroshi Takeyama, *Tokyo*
Koji Tanaka, *Suita*
Kuniya Tanaka, *Yokohama*
Shinji Tanaka, *Tokyo*
Akira Tsunoda, *Kamogawa*
Dai Uematsu, *Nagano*
Shinichi Ueno, *Kagoshima*
Toshifumi Wakai, *Niigata*
Atsushi Watanabe, *Sapporo*
Toshiaki Watanabe, *Tokyo*
Yo-ichi Yamashita, *Hiroshima*
Naohisa Yoshida, *Kyoto*
Seiichi Yoshida, *Niigata*

**Lebanon**

Bishara Atiyeh, *Beirut*

**Lithuania**

Aleksandras Antusevas, *Kaunas*

**Mexico**

José A Robles Cervantes, *Guadalajara*
Miguel F Herrera, *Mexico City*

**Netherlands**

Frans L Moll, *Utrecht*
Paulus Joannes van Diest, *Utrecht*

**Nigeria**

Christopher Olusanjo Bode, *Lagos*

**Norway**

Michael Brauckhoff, Bergen

**Pakistan**

Drshamim Muhammad Shamim, *Karachi*

**Poland**

Lek Nowińska Anna, *Katowice*

**Romania**

Mihai Ciocirlan, *Bucharest*
Adrian Iancu, *Cluj Napoca*

**Saudi Arabia**

Abdul-Wahed Meshikhes, *Dammam*

**Singapore**

Zhi-wei Huang, *Singapore*
Brian K P Goh, *Singapore*

**South Korea**

Sung-Hyuk Choi, *Seoul*
Young Seob Chung, *Seoul*
Dong-Ik Kim, *Seoul*
Choon Hyuck David Kwon, *Seoul*
Ho-Yeon Lee, *Seoul*
In Ja Park, *Seoul*
Sung-Soo Park, *Seoul*

**Spain**

Maria Angeles Aller, *Vallehermoso*
Aniceto Baltasar, *Alcoy*
Bernardo Hontanilla Calatayud, *Pamplona*
Manuel Giner, *Madrid*
Fernando Hernanz, *Cantabria*
Álvaro Larrad Jiménez, *Madrid*
David Martinez-Ramos, *Castellon*
Juan Viñas Salas, *Leida*
Eduardo M Targarona, *Barcelona*
Carmen Peralta Uroz, *Barcelona*
Jesus Vaquero, *Madrid*

**Switzerland**

Marco Buter, *Zürich*
Pascal Gervaz, *Geneva*
Merlin Guggenheim, *Männedorf*
Jürg Metzger, *Lucerne*
Cafarotti Stefano, *Bellinzona*

**Thailand**

Varut Lohsiriwat, *Bangkok*

**Turkey**

Ugur Boylu, *Istanbul*

WJSP

World Journal of Surgical Procedures

Contents

Four-monthly Volume 4 Number 1 March 28, 2014

**Contents**

*World Journal of Surgical Procedures*
**Volume 4 Number 1 March 28, 2014**



**AIM AND SCOPE**

*World Journal of Surgical Procedures* (*World J Surg Proced*, *WJSP*, online ISSN 2219-2832, DOI: 10.5412) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

*WJSP* covers topics concerning ambulatory surgical procedures, cardiovascular surgical procedures, digestive system surgical procedures, endocrine surgical procedures, obstetric surgical procedures, neurosurgical procedures, ophthalmologic surgical procedures, oral surgical procedures, orthopedic procedures, otorhinolaryngologic surgical procedures, reconstructive surgical procedures, thoracic surgical procedures, urogenital surgical procedures, computer-assisted surgical procedures, elective surgical procedures, and minimally invasive, surgical procedures, specifically including ablation techniques, anastomosis, assisted circulation, bariatric surgery, biopsy, body modification, non-therapeutic, curettage, debridement, decompression, deep brain stimulation, device removal, dissection, drainage, electrosurgery, extracorporeal circulation, hemostasis, intraoperative care, laparotomy, ligation, lymph node excision, mastectomy, microsurgery, monitoring, intraoperative, ostomy, paracentesis, pelvic exenteration, perioperative care, postoperative care, preoperative care, prosthesis implantation, reoperation, second-look surgery, splenectomy, suture techniques, symphysiotomy, tissue and organ harvesting, transplantation, diagnostic imaging, and endoscopy.

We encourage authors to submit their manuscripts to *WJSP*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.





NAME OF JOURNAL
*World Journal of Surgical Procedures*

ISSN
ISSN 2219-2832 (online)

LAUNCH DATE
December 29, 2011

FREQUENCY
Four-monthly



Xiu-Xia Song, Vice Director
*World Journal of Surgical Procedures*
Room 903, Building D, Ocean International Center,
No. 62 Dongsihuan Zhonglu, Chaoyang District,
Beijing 100025, China
Telephone: +86-10-85381891
Fax: +86-10-85381893
E-mail: bpgoffice@wjgnet.com
http://www.wjgnet.com

PUBLISHER
Baishideng Publishing Group Co., Limited
Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road, Wan Chai,
Hong Kong, China
Fax: +852-65557188
Telephone: +852-31779906
E-mail: bpgoffice@wjgnet.com
http://www.wjgnet.com

PUBLICATION DATE
March 28, 2014

World Journal of Surgical Procedures

Online Submissions: http://www.wjgnet.com/esps/
bpgoffice@wjgnet.com
doi:10.5412/wjsp.v4.i1.1

*World J Surg Proced* 2014 March 28; 4(1): 1-8
ISSN 2219-2832 (online)


MINIREVIEWS

# Outcomes of continuous flow ventricular assist devices

Shelly Bansal, Chittoor B Sai-Sudhakar, Bryan A Whitson

Shelly Bansal, Division of Thoracic Transplantation, Department of Cardiothoracic Surgery, University of Pittsburgh, Pittsburgh, PA 15260, United States
Chittoor B Sai-Sudhakar, Division of Cardiac Surgery, Department of Surgery, The Ohio State University, Columbus, OH 43210, United States
Bryan A Whitson, Division of Cardiac Surgery, The Collaboration for Organ Perfusion, Protection, Engineering and Regeneration (COPPER) Laboratory, The Ohio State University Wexner Medical Center, Columbus, OH 43210, United States
Author contributions: Bansal S, Sai-Sudhakar CB, and Whitson BA contributed equally to this works authorship and revision.
Correspondence to: Bryan A Whitson, MD, PhD, Division of Cardiac Surgery, The Collaboration for Organ Perfusion, Protection, Engineering and Regeneration (COPPER) Laboratory, The Ohio State University Wexner Medical Center, N-813 Doan Hall, 410 W. 10th Ave., Columbus, OH 43210,
United States. bryan.whitson@osumc.edu
Telephone: +1-614-3667414 Fax: +1-614-2932020
Received: November 29, 2013 Revised: January 14, 2014
Accepted: January 17, 2014
Published online: March 28, 2014

## Abstract

Heart transplantation is commonplace, the supply is limited. Many exciting changes in the field of mechanical circulatory support have occurred in the past few years, including the axial flow pump. Left ventricular assist device (LVAD) therapy is ever evolving. As the use of LVAD therapy increases it is important to understand the indications, surgical considerations and outcomes.



**Key words:** Left ventricular assist device; Axial flow; Mechanical circulatory support; Heart failure; Continuous flow

**Core tip:** Left ventricular assist devices provide a durable, long-term alternative to heart transplant for those with end-stage heart failure. In an era of limited transplant donor supply, axial flow pumps are a viable alternative.

Bansal S, Sai-Sudhakar CB, Whitson BA. Outcomes of continuous flow ventricular assist devices. *World J Surg Proced* 2014; 4(1): 1-8 Available from: URL: http://www.wjgnet.com/2219-2832/full/v4/i1/1.htm DOI: http://dx.doi.org/10.5412/wjsp.v4.i1.1

## INTRODUCTION AND OVERVIEW

It is estimated that 5 million individuals are affected by heart failure. In general patients with heart failure have a poor prognosis and while cardiac transplantation is an effective long-term therapy for a select group of patients, the number of transplants have plateaued[1]. While pharmacologic therapy and cardiac resynchronization have improved symptoms and survival in heart failure patients, the survival for patients on inotropes is approximately 6% at 12 mo[2,3]. Due to the severe organ shortage and marginal improvements in outcomes with medical management alternate therapies such as mechanical circulatory support have developed. Since the first generation pulsatile pumps were developed approximately 50 years ago, improvements have been made to the design and have largely been replaced by axial pumps[4]. This article will review mechanical circulatory support, specifically left ventricular assist device (LVAD) axial flow pumps, and indications for use, surgical considerations and outcomes.

### *History of axial pumps*

The first sets of pumps were developed over fifty years ago at the National Heart, Lung and Blood institute[4]. First generation pumps were pulsatile and included the Heartmate XVE and Novacor device. Originally placed as a bridge to transplant, the REMATCH trial showed an unprecedented improvement in early survival compared to conventional therapy and they were approved for destination therapy[5]. In 2009, Slaughter *et al*[6] showed

significantly better survival for axial flow pumps, 68% at 1 year and 58% at 2 years. These findings resulted in a significant change in practice and increased the use of axial flow pumps by tenfold[4].

### Pump mechanics

Compared to pulsatile devices, axial flow pumps are smaller in size and easier to implant. In addition they have a singular moving part, making axial flow pumps more reliable with a lower adverse event profile. Axial flow pumps have a blood inlet and an outlet. A single internal rotor or impeller continuously unloads the left ventricle propelling blood in the axial direction. The impeller is kept within a rigid house. There are several bearing designs that drive the impeller, which include mechanical/pivot design, hydrodynamics, electromagnetic or a permanent magnet[7].

In an axial flow pump, mechanics are based on preload, speed at which the impeller rotates and afterload. For example, as the blood volume decreases, such as in hemorrhagic shock, the pump will continue to flow and the ventricle will collapse and result in inlet obstruction. In contrast, the patient might be volume overloaded and the speed of the pump might be inadequate to unload the ventricle resulting in signs and symptoms of heart failure.

Axial flow pumps are sensitive to afterload and this can have a profound impact on the flow mechanics. As the blood pressure increases the impeller has to increase its power to generate rotation in an attempt to maintain the constant rotations per minute (rpm). With an increased afterload, even at a set rpm, the increased afterload causes decrease in flows and hemodynamic support[8]. In this scenario the pulsatility index (PI) will be elevated and the flows will be decreased. It is therefore important to control blood pressure in the acute and outpatient setting.

Axial flow pumps run by setting the speed of the impeller, or rpm. Pump speeds are based on the patient's clinical status, volume status and echocardiographic findings[8]. The monitor provides information on speed, power, PI and calculated flows. The monitor can alert clinicians about proper pump function and changes in the PI or power may be a result of pump malfunction or a change in clinical status.

To summarize, axial flow pumps are durable pumps with a 58% survival at 2 years for destination therapy. Long term durability is attributed to minimal friction and heat production. Pump function is based on the patient's clinical status and pump speed. And finally due to continuous blood flow patients lack a pulse and may require Doppler blood pressure measurement.

### How long have they been used

Axial flow pumps went into trial in 2003. Primary endpoints for bridge to transplant (BTT) patients included rate of survival to transplant or survival at 180 d. The primary endpoint for destination therapy patients was a composite endpoint at 2 years that included survival, adverse events and pump durability. The study found improved survival rates, improvement in quality of life and functional status in both groups. Axial flow devices, specifically the Heartmate Ⅱ, were approved by the Food and Drug Administration in 2008 as a bridge to transplant and in 2010 as destination therapy[9]. Since then a more recent review of outcomes for destination therapy demonstrates 74% survival at one year[10].

## TYPES OF USE

Second generation and third generation axial flow devices have a high degree of reliability. This has resulted in a tenfold increase in their use[4]. Current indications include, myocardial recovery, BTT, bridge to decision and destination therapy. Device strategy is dependent on the patient's clinical status, co morbidities, end organ dysfunction and social support.

### Bridge to recovery

Very few patients after LVAD placement will have myocardial recovery. A recent analysis of approximately 1100 Heartmate Ⅱ patients showed a 1.8% rate of recovery[11]. In a few, long term left ventricular unloading may provide reversal of atrophy in the cardiomyocytes and recovery of left ventricular geometry and function[12]. One such strategy includes the addition of pharmacological therapy to patients with continuous flow devices, to promote reverse remodeling. Birks *et al*[13] showed in a small group of patients the addition of high dose ACE inhibitors, beta blockers plus clenbuterol promotes myocardial recovery. While much is unknown about myocardial recovery after LVAD implantation, a considerable amount of research is being performed in this area.

### Bridge to decision

Patients receiving mechanical circulatory support prior to determining eligibility for transplant are considered bridge to decision. In these patients end organ dysfunction including pulmonary hypertension, renal failure, obesity, medical compliance, tobacco abuse can be absolute or temporary contraindications for heart transplant. For a few of these patients, organ dysfunction will be reversible with mechanical circulatory support or afford them the opportunity to modify lifestyle making them eligible for transplantation.

### Bridge to transplant

Bridges to transplant are patients who are eligible for cardiac transplant but have had progression of their disease. On any given day, there are 3000 patients on the waitlist per day, since survival is poor, approximately 43% will require mechanical circulatory support to "bridge" them until an organ is available[14]. The goal is to prevent end organ dysfunction for continued eligibility. Additionally, during that wait-list time, the patient is able to be out of the hospital, enjoying a reasonable quality of life and gaining strength and conditioning.

The use of LVAD therapy in candidates for heart

transplant is not benign and careful consideration should be made regarding the risks and benefits. While LVAD therapy will support end-organ function and improve quality of life, LVAD therapy will require an additional sternotomy for placement and redo sternotomy at the time of transplant. Additional concerns include blood transfusions at the time of placement, infections, stroke, and complications with the pump.

### Destination therapy

Most patients in heart failure are not candidates for transplantation. Without advanced therapy, many will die within a year or continue to have poor function and quality of life.

The REMATCH trial was the first study to compare mechanical circulatory support to medical management. In this landmark trial the survival rate was 52% in the patients receiving mechanical circulatory support and 23% in the medical management group[5]. In 2002 the first generation pumps were approved and in 2010 the second-generation pump was approved for destination therapy. Since then the survival rates have improved and mechanical circulatory support provides patients equivalent survival to transplant patients at one year[6,15].

With the support of LVAD's, destination therapy patients have improved quality of life and improvement in their function. A study from Rogers *et al*[16] reported on functional capacity and quality of life of patients under long-term LVAD support. NYHA functional class, 6-min walk distance, patient activity scores as well as quality of life (Minnesota Living With Heart Failure and Kansas City Cardiomyopathy Questionnaires) were collected before and after LVAD implantation. Following implant, 80% of destination treatment patients at 6 mo and 79% at 24 mo improved to NYHA functional class I or Ⅱ. Mean 6-min walk distance in these patients was 204 m in patients able to ambulate at baseline, which improved to 350 and 360 m at 6 and 24 mo. There were also significant and sustained improvements from baseline in both quality of life scores. The relative bridge to recovery is minimal between indications.

## TYPES OF PUMPS

### Heartmate Ⅱ

The Heartmate Ⅱ is a continuous axial flow device. It contains an internal rotor with helical blades that curve around a central shaft. As blood enters the chamber the internal blade rotates and converts the radial velocity of the blood flow to an axial direction, hence the term axial pump. The pump weighs 350 g and can flow up to 10 L/min. The inflow cannula is placed in the left ventricle apex and the outflow graft is connected to the ascending aorta. Due to pump size the pump housing is placed in the left upper quadrant in the pre-peritoneal pocket. The device is connected to controller *via* a driveline that is tunneled thru the subcutaneous tissue and brought out to the skin.

### Jarvik 2000

The Jarvik 2000 is a continuous flow pump that unlike the Heartmate Ⅱ is placed within the left ventricle. It weighs approximately 85 g. A single impeller is housed within titanium housing completely inside the ventricle. Interestingly the outflow can be connected to either the ascending or descending aorta. The pump flows up to 7 L/min. One added benefit of the Jarvik pump is the skull mounted driveline. Unlike other pumps the skull implant is designed to be resistant to infection and allows patients to shower, bath or swim[17].

### INCOR

The INCOR is a continuous axial flow pump developed by Berlin Heart. The INCOR design is slightly different in that the impeller is levitated by an electromagnetic bearing and therefore the parts do not come in contact with each other. The lack of contact improves long-term durability by decreasing heat and friction. The pump can flow up to 6 L/min. The INOR is currently not available in the United States[18].

### Micromed debakey

The Micromed Debakey is a fully implantable electromagnetic axial flow pump. The pump weighs 93 g. Due to its small size it can be placed in the intra-pericardial position. The pump consists of an inflow cannula, apical ring, the pump, and outflow graft. A flow probe encircles the outflow graft providing real-time cardiac output. The pump can flow up to 5 L/min. The pump is connected thru a driveline to a controller module and runs off 12-volt DC batteries for 4 to 6 h[19].

## TECHNICAL CONSIDERATIONS

### Aortic insufficiency

Pre-operative aortic insufficiency (AI) is important to identify in LVAD patients. Patients with greater than moderate aortic insufficiency prior to implant should be surgically treated at the time LVAD implant. Since the ventricle does not contract the ventricle fills during the cardiac cycle creating a circular loop[20]. Since the left ventricle does not have time to unload this may affect the long term durability of the pump. More importantly aortic insufficiency leads to high pump flows and low total cardiac output[21]. For patients with mild AI who are undergoing LVAD placement for long term support the AI may progress over time and should be monitored. Cowger *et al*[22] found that patients supported at 18 mo had moderate or worse AI and half the individuals with moderate or worse AI required readmission for heart failure or an arrhythmia. They pointed out that while the long-term significance is not known increase in AI might have real clinical impact on long-term mechanical support.

A second group of patients develop AI over time due to degeneration or fusion of the leaflets. Since patients with LVAD's have minimal or no pulse in the native LV,

although contracting the LV may not generate enough pressure to open the aortic valve. The lack of pulse is implicated in postoperative AI[23]. Decreasing pump speed may reduce the transvalvular gradient and temporarily improve systemic perfusion especially in patients who develop AI after LVAD placement. But this may be temporary solution. More durable options include the Park stitch, over sewing of the valve with patch, or replacement with a tissue valve, but come with increased morbidity.

Surgical options for the treatment of aortic insufficiency include repair or replacement of the aortic valve. The Park stitch is described as a central coaptation stitch has been shown to be a durable option up to two years after LVAD placement[24]. Another option includes over sewing of the outflow tract and keeping the valve leaflets intact. Patients with an over sewn aortic valve are completely dependent on the LVAD. If an aortic valve replacement is needed, a tissue valve is preferred. Mechanical valves leave patients with increased risk of thromboembolic phenomena, since the lack of ventricular contraction leads to sub valvular thrombus formation and stasis around the struts.

### Mechanical aortic valve

Preexisting mechanical aortic valves are considered a relative contraindication to LVAD placement. Leaving a mechanical aortic valve leaflets patients at higher risk of thromboembolic complications and the possibility that the valve could remain in the open position. Replacement of mechanical valve at the time of LVAD operation increases pump times and may not be tolerated in sicker patient. Therefore careful consideration should be made when placing LVAD's in this patient population[25].

### Mitral regurgitation

In most cases mitral regurgitation does not need to be corrected at the time of implantation. Once the LV is decompressed, in most cases mitral insufficiency can be managed by increasing or decreasing pump speed. In a few patients, specifically BTT candidates, the addition of a mitral valve regurgitation may result in a decrease in pulmonary vascular resistance (PVR) and may permit certain patients thought to be ineligible for transplantation to become candidates[26]. It should be noted that patients with myocardial recovery who undergo LVAD explanation might need an additional operation for mitral insufficiency at the time of device explant.

### Tricuspid regurgitation

Tricuspid regurgitation in patients with right heart dysfunction is associated with poor prognosis[27]. Continued tricuspid regurgitation after LVAD may progress after LV decompression, resulting in further annular dilatation and right ventricular (RV) failure. Also there is increased operative mortality in patients undergoing isolated redo tricuspid valve (TV) operation especially in the face of worsening right heart failure. While there are increased cardiopulmonary bypass times in patients who undergo concomitant TV repair/replacement, repair/or replacement of the TV at the time of implantation results in improved short term results including less RV failure and may promote remodeling of the RV[23,28].

### Patent foramen ovale

Investigations for a patent foramen ovale (PFO) should be performed prior to LVAD implantation. Imaging studies include surface or trans esophageal echocardiography combined with "bubble study" and concurrent color Doppler. Patients can perform a Valsalva maneuver with release to identify hidden PFO's. Doppler echocardiography may show a left to right shunt, but the bubble study may not reveal a PFO in the setting of high elevated left atrial pressures[21]. After LVAD implantation, unloading of the left ventricle may uncover a PFO. Patients may present with stroke or pump thrombosis. One of more common consequences of a PFO includes the development of severe hypoxia due to a right to left shunt, making it important to identify prior to LVAD implantation[21].

### Mitral stenosis

Mitral stenosis is a bigger problem for patients undergoing LVAD placement[29]. Mitral stenosis limits left ventricular filling and limit pump flows[30]. In addition, the persistently elevated left atrial pressure lead to continued pulmonary hypertension. Treatment options include commisurotomy or tissue replacement[8].

### Ventricular tachycardia

Ventricular tachycardia (VT) is common in patients with heart failure. Most patients undergoing LVAD's already have an implantable defibrillator at the time of the surgery. Despite ventricular unloading many patients continue to have VT. Reversible and non-reversible causes of VT should be determined since continued VT after LVAD placement can lead to inadequate systemic perfusion. Reversible causes include suction events or cannula position. Patients with irreversible causes should be managed with pharmacological therapies and or catheter ablation[31]. A unique option includes scar mapping and ablation for resistant ventricular arrhythmias. A recent series by Cantillon *et al*[32] showed that out of 32 diagnostic and ablation procedures out of 611 LVAD implantations, the dominant mechanism was intrinsic myocardial scar, with only 14% of VT circuits involving the apical inflow cannulation site. Ablation was acutely successful (VT non-inducible) in 86% of patients, with freedom from recurrent VT of 67% during a mean duration of LVAD support of 120 d.

## DURABILITY OF PUMP

Pump technology has improved significantly since the original pulsatile devices. The current second generation pumps have an estimated clinical life of greater than 5 years. Due to improved durability we are now seeing a different number of adverse events.

### Complications

Thrombosis and bleeding are common complications in patients with mechanical circulatory support. Patients with LVADs are prone to thrombosis due to the blood device interaction. In order to prevent this patients are maintained on a regimen of coumadin and antiplatelet agents. The current rates of pump thrombosis is anywhere from 0.014 to 0.03 events per patient-year and actually may be increasing in incidence[33]. Pump thrombosis is a difficult problem to diagnose and even more difficult to treat. Laboratory monitoring of lactate dehydrogenase, plasma free hemoglobin and increased pump power alert physicians to pump thrombus but additional studies such as RAMP protocols help to diagnose thrombus. The question remains how best to treat the problem. Increase in pump speed, change in international normalized ratio goals, or additional antiplatelet agents may help to resolve the pump thrombosis. Ultimately some patients will have to their pump changed out due to the thrombosis; which comes with and increased morbidity and mortality.

### Bleeding

Bleeding is another common problem seen in patients with LVAD's. The combination of anticoagulation and acquired hematologic problems due to device flow characteristics results in a bleeding diathesis. Bleeding is a significant problem and results in 3% mortality from bleeding complications[34]. Gastrointestinal bleeding is a long been recognized complication of axial flow pumps. Acquired von Willebrand syndrome or distention of submucosal venous plexus from diminished pulsatility is thought to be a key event. An attempt at decreasing pump speeds to restore pulsatility and stop the destruction of large von willebrand factor multimers may be of benefit[34]. Other treatment options include epinephrine or octreotide. For patients with recalcitrant bleeding, long-term cessation of anticoagulation or surgical management of the culprit gastrointestinal tract lesion has also been used.

### Stroke

The incidence of stroke after LVAD placement is reported to be 8.0% to 25.0%[35]. Depending on the anticoagulation regimen, antiplatelet regimen and device type the stroke rates will vary[36]. Approximately a third of ischemic strokes will convert to a hemorrhagic stroke.

### Infection

Infection remains a considerable complication with LVAD patients. Infections can be grouped into three categories; VAD specific, VAD related or non-VAD related infections[37]. Of the VAD specific infections, pocket infections occur in ten percent of the population. Driveline infections are a much larger problem in the LVAD population. The rate of infection is somewhere between 0.37-0.58 events per patient year. Driveline infections are generally related to driveline movement. Chronic movement prevent in growth of tissue into the external velour layer of the driveline. Once a driveline infection is suspected, treatment should include both systemic and local antibiotics. It is important to note that infections in the LVAD patients may lead to pump infections, bacteremia and even more worrisome pump thrombosis[33].

### Pump failure

The newer second generation are estimated to have long-term clinical durability; greater than 5 years[7]. But with increased wear and tear it exposes the LVAD to device related problems. Failure of the controller and power source are rare. The most susceptible to damage is the external driveline due to tugging, twisting or kinking. The estimated rate is approximately 0.03 events per patient year[38]. In most cases of pump failure, patients are trained on trouble shooting the controller and power source.

### Brief comparison compared to heart failure

The REMATCH trial evaluated the efficacy and safety of long-term left ventricular assist device support chronic end-stage heart failure patients. Compared with optimal medical management, LVAD implantation significantly improved the survival and quality of life. Favorable results in this bridge to transplant population encouraged the design of the multicenter REMATCH trial to evaluate the efficacy and safety of long-term LVAD support. Compared with optimal medical management ($n$ = 61), LVAD implantation ($n$ = 68) doubled the 1-year survival rate (from 25% to 51%). While the original trial compared first generation pumps to medical management, the outcomes with LVADS were superior. At two years the survival was 23% compared to 8% in the medical therapy group. Functional status and quality of life were improved at one year in the LVAD group[5]. A second study comparing first generation devices to the current axial flow devices showed improved survival. One-year survival was 68% and 58% at the second year compared to original REMATCH trial results[6].

## EFFECTS ON PHYSIOLOGY

### End organ perfusion

An animal study using the Terumo DuraHeart LVAD, an axial flow device, found an increase in the plasma renin levels without a significant increase in the blood pressure despite the up regulation[39]. But the clinical relevance is unknown. More work is needed to evaluate and closely study the effect of continuous-flow devices in select populations of heart failure patients, such as those with baseline severe multisystem organ failure. In addition, longer-term studies are needed to assess end-organ function with continuous-flow devices, which may have important implications for use as destination therapy[40].

### Renal failure

Forty five percent of patients with heart failure have associated renal dysfunction. Cardiorenal syndrome is related to low output and low flow to the kidneys and venous hypertension. Since chronic kidney disease is a relative contraindication to heart transplant, patients with heart failure and renal dysfunction may be candidates for

destination therapy. LVAD therapy improves forward flow and improves renal function in a large proportion of patients. Initial improvements can be seen in the first month, but plateaus thereafter. The implantation of LVAD therapy might help differentiate reversible and irreversible renal dysfunction in heart failure[41].

### PA pressures

Fixed pulmonary hypertension is a contra indication for patients with heart failure. Many times it is unclear if pulmonary hypertension is due to left ventricular failure or intrinsic lung disease. Generally these patients will have a transpulmonary gradient greater than 14 mmHg and a pulmonary vascular resistance greater than 3 Wood units. For patients with reversible pulmonary hypertension, unloading of the left ventricle may decrease pulmonary hypertension. A study from John *et al*[42] showed improvement in mean pulmonary pressures and improvement in PVR. While the improvements in pulmonary artery pressures are seen in the first 6 mo, the changes in pulmonary pressures plateau. The hemodynamic changes in pulmonary artery pressures appear to persist after heart transplant.

### Right ventricle

After LVAD placement, end organ perfusion improves and there may be a drastic decrease in afterload of the pulmonary circulation. In some patients this is beneficial, but in a third of patients this will result in right ventricular failure. Hannan *et al*[37] looked at the outcomes of right ventricular failure after LVAD placement. Overall, 30 (6%) patients receiving left ventricular assist devices required a right ventricular assist device, 35 (7%) required extended inotropes, and 33 (7%) required late inotropes. A significantly greater percentage of patients without right ventricular failure survived to transplantation, recovery, or ongoing device support at 180 d compared with patients with right ventricular failure. They concluded that right ventricular failure is associated with worse outcomes than without. An extremely difficult problem to manage both medically and surgically, acute RV failure comes with high short and long term mortality. Predicting RV failure is difficult. Optimizing volume status, decreasing pulmonary pressures and the addition of inotropes is important. Post operatively the use of inhaled nitric oxide and pulmonary vasodilators will help to augment right ventricular function.

### Coagulation

Recent reports have indicated that there may be an increase in the relative rate of thrombosis of axial flow devices[43]. The exact etiology of this observation is unknown but does make one more aware of the need for meticulous attention to anticoagulation in these implantable devices with a continuous blood interface.

## SUMMARY/OVERVIEW

Although heart transplantation is commonplace, the supply is limited. Many exciting changes in the field of mechanical circulatory support have occurred in the past few years, including the axial flow pump. LVAD therapy is ever evolving. As the use of LVAD therapy increases it is important to understand the indications, surgical considerations and outcomes.

## REFERENCES


1 **Long JW**, Kfoury AG, Slaughter MS, Silver M, Milano C, Rogers J, Delgado R, Frazier OH. Long-term destination therapy with the HeartMate XVE left ventricular assist device: improved outcomes since the REMATCH study. *Congest Heart Fail* 2005; **11**: 133-138 [PMID: 15947534 DOI: 10.1111/j.1527-5299.2005.04540.x]

2 **Hershberger RE**, Nauman D, Walker TL, Dutton D, Burgess D. Care processes and clinical outcomes of continuous outpatient support with inotropes (COSI) in patients with refractory endstage heart failure. *J Card Fail* 2003; **9**: 180-187 [PMID: 12815567 DOI: 10.1054/jcaf.2003.24]

3 **Kass DA**. Cardiac resynchronization therapy. *J Cardiovasc Electrophysiol* 2005; **16** Suppl 1: S35-S41 [PMID: 16138884 DOI: 10.1111/j.1540-8167.2005.50136.x]

4 **Stewart GC**, Stevenson LW. Keeping left ventricular assist device acceleration on track. *Circulation* 2011; **123**: 1559-1568; discussion 1568 [PMID: 21482974 DOI: 10.1161/CIRCULATIONAHA.110.982512]

5 **Rose EA**, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, Long JW, Ascheim DD, Tierney AR, Levitan RG, Watson JT, Meier P, Ronan NS, Shapiro PA, Lazar RM, Miller LW, Gupta L, Frazier OH, Desvigne-Nickens P, Oz MC, Poirier VL. Long-term use of a left ventricular assist device for end-stage heart failure. *N Engl J Med* 2001; **345**: 1435-1443 [PMID: 11794191 DOI: 10.1056/NEJMoa012175]

6 **Slaughter MS**, Rogers JG, Milano CA, Russell SD, Conte JV, Feldman D, Sun B, Tatooles AJ, Delgado RM, Long JW, Wozniak TC, Ghumman W, Farrar DJ, Frazier OH. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med* 2009; **361**: 2241-2251 [PMID: 19920051 DOI: 10.1056/NEJMoa0909938]

7 **Moazami N**, Fukamachi K, Kobayashi M, Smedira NG, Hoercher KJ, Massiello A, Lee S, Horvath DJ, Starling RC. Axial and centrifugal continuous-flow rotary pumps: a translation from pump mechanics to clinical practice. *J Heart Lung Transplant* 2013; **32**: 1-11 [PMID: 23260699 DOI: 10.1016/j.healun.2012.10.001]

8 **Slaughter MS**, Pagani FD, Rogers JG, Miller LW, Sun B, Russell SD, Starling RC, Chen L, Boyle AJ, Chillcott S, Adamson RM, Blood MS, Camacho MT, Idrissi KA, Petty M, Sobieski M, Wright S, Myers TJ, Farrar DJ. Clinical management of continuous-flow left ventricular assist devices in advanced heart failure. *J Heart Lung Transplant* 2010; **29**: S1-S39 [PMID: 20181499 DOI: 10.1016/j.healun.2010.01.011]

9 **Pagani FD**, Miller LW, Russell SD, Aaronson KD, John R, Boyle AJ, Conte JV, Bogaev RC, MacGillivray TE, Naka Y, Mancini D, Massey HT, Chen L, Klodell CT, Aranda JM, Moazami N, Ewald GA, Farrar DJ, Frazier OH. Extended mechanical circulatory support with a continuous-flow rotary left ventricular assist device. *J Am Coll Cardiol* 2009; **54**: 312-321 [PMID: 19608028 DOI: 10.1016/j.jacc.2009.03.055]

10 **Slaughter MS**, Rogers JG, Milano CM. Destination therapy: Improving outcomes with continuous flow LVAD's. *ISHLT* 2010

11 **Maybaum S**. Cardiac recovery during continuous-flow left ventricular assist device support: some good news from across the Atlantic. *Circulation* 2011; **123**: 355-357 [PMID: 21242486 DOI: 10.1161/CIRCULATIONAHA.110.005199]

12 **Guglin M**, Miller L. Myocardial recovery with left ventricular assist devices. *Curr Treat Options Cardiovasc Med* 2012; **14**:

370-383 [PMID: 22760582 DOI: 10.1007/s11936-012-0190-9]
13 **Birks EJ**, Tansley PD, Hardy J, George RS, Bowles CT, Burke M, Banner NR, Khaghani A, Yacoub MH. Left ventricular assist device and drug therapy for the reversal of heart failure. *N Engl J Med* 2006; **355**: 1873-1884 [PMID: 17079761 DOI: 10.1056/NEJMoa053063]
14 **Peura JL**, Colvin-Adams M, Francis GS, Grady KL, Hoffman TM, Jessup M, John R, Kiernan MS, Mitchell JE, O' Connell JB, Pagani FD, Petty M, Ravichandran P, Rogers JG, Semigran MJ, Toole JM. Recommendations for the use of mechanical circulatory support: device strategies and patient selection: a scientific statement from the American Heart Association. *Circulation* 2012; **126**: 2648-2667 [PMID: 23109468 DOI: 10.1161/CIR.0b013e3182769a54]
15 **Lahpor J**, Khaghani A, Hetzer R, Pavie A, Friedrich I, Sander K, Strüber M. European results with a continuous-flow ventricular assist device for advanced heart-failure patients. *Eur J Cardiothorac Surg* 2010; **37**: 357-361 [PMID: 19616963]
16 **Rogers JG**, Aaronson KD, Boyle AJ, Russell SD, Milano CA, Pagani FD, Edwards BS, Park S, John R, Conte JV, Farrar DJ, Slaughter MS. Continuous flow left ventricular assist device improves functional capacity and quality of life of advanced heart failure patients. *J Am Coll Cardiol* 2010; **55**: 1826-1834 [PMID: 20413033 DOI: 10.1016/j.jacc.2009.12.052]
17 Available from: URL: http://www.jarvikheart.com
18 Available from: URL: http://www.berlinheart.de/index.php/home
19 **Goldstein DJ**. Worldwide experience with the MicroMed DeBakey Ventricular Assist Device as a bridge to transplantation. *Circulation* 2003; **108** Suppl 1: II272-II277 [PMID: 12970245 DOI: 10.1161/01.cir.0000087387.02218.7e]
20 **Felix SE**, Martina JR, Kirkels JH, Klöpping C, Nathoe H, Sukkel E, Hulstein N, Ramjankhan FZ, Doevendans PA, Lahpor JR, de Jonge N. Continuous-flow left ventricular assist device support in patients with advanced heart failure: points of interest for the daily management. *Eur J Heart Fail* 2012; **14**: 351-356 [PMID: 22308012 DOI: 10.1093/eurjhf/hfs012]
21 **Topilsky Y**, Hasin T, Oh JK, Borgeson DD, Boilson BA, Schirger JA, Clavell AL, Frantz RP, Tsutsui R, Liu M, Maltais S, Kushwaha SS, Pereira NL, Park SJ. Echocardiographic variables after left ventricular assist device implantation associated with adverse outcome. *Circ Cardiovasc Imaging* 2011; **4**: 648-661 [PMID: 21940507 DOI: 10.1161/CIRCIMAGING.111.965335]
22 **Cowger J**, Pagani FD, Haft JW, Romano MA, Aaronson KD, Kolias TJ. The development of aortic insufficiency in left ventricular assist device-supported patients. *Circ Heart Fail* 2010; **3**: 668-674 [PMID: 20739615 DOI: 10.1161/CIRCHEARTFAILURE.109.917765]
23 **Milano CA**, Simeone AA. Mechanical circulatory support: devices, outcomes and complications. *Heart Fail Rev* 2013; **18**: 35-53 [PMID: 22395673 DOI: 10.1007/s10741-012-9303-5]
24 **McKellar SH**, Deo S, Daly RC, Durham LA, Joyce LD, Stulak JM, Park SJ. Durability of central aortic valve closure in patients with continuous flow left ventricular assist devices. *J Thorac Cardiovasc Surg* 2014; **147**: 344-348 [PMID: 23246052]
25 **Dranishnikov N**, Stepanenko A, Potapov EV, Dandel M, Siniawski H, Mladenow A, Hübler M, Grauhan O, Weng Y, Krabatsch T, Hetzer R, Kukucka M. Simultaneous aortic valve replacement in left ventricular assist device recipients: single-center experience. *Int J Artif Organs* 2012; **35**: 489-494 [PMID: 22661109 DOI: 10.5301/ijao.5000102]
26 **Taghavi S**, Hamad E, Wilson L, Clark R, Jayarajan SN, Uriel N, Goldstein DJ, Takayama H, Naka Y, Mangi AA. Mitral valve repair at the time of continuous-flow left ventricular assist device implantation confers meaningful decrement in pulmonary vascular resistance. *ASAIO J* 2013; **59**: 469-473 [PMID: 23896769 DOI: 10.1097/MAT.0b013e31829be026]
27 **Pinney SP**. The role of tricuspid valve repair and replacement in right heart failure. *Curr Opin Cardiol* 2012; **27**: 288-295 [PMID: 22327290 DOI: 10.1097/HCO.0b013e3283512051]
28 **Piacentino V**, Troupes CD, Ganapathi AM, Blue LJ, Mackensen GB, Swaminathan M, Felker GM, Stafford-Smith M, Lodge AJ, Rogers JG, Milano CA. Clinical impact of concomitant tricuspid valve procedures during left ventricular assist device implantation. *Ann Thorac Surg* 2011; **92**: 1414-1418; discussion 1414-1418; [PMID: 21958790 DOI: 10.1016/j.athoracsur.2011.05.084]
29 **Northern LR**, Dhawan R, Petra Bas H, Vidal-Melo MF, Mohr FW, Garbade J. CASE 1-2014 Left Ventricular Assist Device Insertion and the Mitral Valve. *J Cardiothorac Vasc Anesth* 2014; **28**: 174-180 [PMID: 23938398]
30 **Mohite PN**, Zych B, Popov AF, Patil N, Luthra S, Hedger M, Simon AR, Amrani M. Mitral commissurotomy through the left ventricle apical orifice with Heart Ware left ventricular assist device implantation. *J Cardiothorac Surg* 2013; **8**: 147 [PMID: 23758964]
31 **Nakahara S**, Chien C, Gelow J, Dalouk K, Henrikson CA, Mudd J, Stecker EC. Ventricular arrhythmias after left ventricular assist device. *Circ Arrhythm Electrophysiol* 2013; **6**: 648-654 [PMID: 23778248 DOI: 10.1161/CIRCEP.113.000113]
32 **Cantillon DJ**, Bianco C, Wazni OM, Kanj M, Smedira NG, Wilkoff BL, Starling RC, Saliba WI. Electrophysiologic characteristics and catheter ablation of ventricular tachyarrhythmias among patients with heart failure on ventricular assist device support. *Heart Rhythm* 2012; **9**: 859-864 [PMID: 22293139 DOI: 10.1016/j.hrthm.2012.01.018]
33 **Goldstein DJ**, John R, Salerno C, Silvestry S, Moazami N, Horstmanshof D, Adamson R, Boyle A, Zucker M, Rogers J, Russell S, Long J, Pagani F, Jorde U. Algorithm for the diagnosis and management of suspected pump thrombus. *J Heart Lung Transplant* 2013; **32**: 667-670 [PMID: 23796150 DOI: 10.1016/j.healun.2013.05.002]
34 **Eckman PM**, John R. Bleeding and thrombosis in patients with continuous-flow ventricular assist devices. *Circulation* 2012; **125**: 3038-3047 [PMID: 22711669]
35 **Kato TS**, Ota T, Schulze PC, Farr M, Jorde U, Takayama H, Naka Y, Yamashita T, Mancini DM. Asymmetric pattern of cerebrovascular lesions in patients after left ventricular assist device implantation. *Stroke* 2012; **43**: 872-874 [PMID: 22207509 DOI: 10.1161/STROKEAHA.111.639682]
36 **Backes D**, van den Bergh WM, van Duijn AL, Lahpor JR, van Dijk D, Slooter AJ. Cerebrovascular complications of left ventricular assist devices. *Eur J Cardiothorac Surg* 2012; **42**: 612-620 [PMID: 22659892 DOI: 10.1093/ejcts/ezs320]
37 **Hannan MM**, Husain S, Mattner F, Danziger-Isakov L, Drew RJ, Corey GR, Schueler S, Holman WL, Lawler LP, Gordon SM, Mahon NG, Herre JM, Gould K, Montoya JG, Padera RF, Kormos RL, Conte JV, Mooney ML. Working formulation for the standardization of definitions of infections in patients using ventricular assist devices. *J Heart Lung Transplant* 2011; **30**: 375-384 [PMID: 21419995 DOI: 10.1016/j.healun.2011.01.717]
38 **Yuan N**, Arnaoutakis GJ, George TJ, Allen JG, Ju DG, Schaffer JM, Russell SD, Shah AS, Conte JV. The spectrum of complications following left ventricular assist device placement. *J Card Surg* 2012; **27**: 630-638 [PMID: 22978843]
39 **Saito S**, Westaby S, Piggot D, Dudnikov S, Robson D, Catarino PA, Clelland C, Nojiri C. End-organ function during chronic nonpulsatile circulation. *Ann Thorac Surg* 2002; **74**: 1080-1085 [PMID: 12400749 DOI: 10.1016/S0003-4975(02)03846-8]
40 **John R**, Boyle A, Pagani F, Miller L. Physiologic and pathologic changes in patients with continuous-flow ventricular assist devices. *J Cardiovasc Transl Res* 2009; **2**: 154-158 [PMID: 20559982 DOI: 10.1007/s12265-009-9092-y]
41 **Hasin T**, Topilsky Y, Schirger JA, Li Z, Zhao Y, Boilson BA, Clavell AL, Rodeheffer RJ, Frantz RP, Edwards BS, Pereira NL, Joyce L, Daly R, Park SJ, Kushwaha SS. Changes in renal function after implantation of continuous-flow left ventricular assist devices. *J Am Coll Cardiol* 2012; **59**: 26-36 [PMID:

22192665 DOI: 10.1016/j.jacc.2011.09.038]

42 **John R**, Liao K, Kamdar F, Eckman P, Boyle A, Colvin-Adams M. Effects on pre- and posttransplant pulmonary hemodynamics in patients with continuous-flow left ventricular assist devices. *J Thorac Cardiovasc Surg* 2010; **140**: 447-452 [PMID: 20435321 DOI: 10.1016/j.jtcvs.2010.03.006]

43 **Starling RC**, Moazami N, Silvestry SC, Ewald G, Rogers JG, Milano CA, Rame JE, Acker MA, Blackstone EH, Ehrlinger J, Thuita L, Mountis MM, Soltesz EG, Lytle BW, Smedira NG. Unexpected abrupt increase in left ventricular assist device thrombosis. *N Engl J Med* 2014; **370**: 33-40 [PMID: 24283197 DOI: 10.1056/NEJMoa1313385]

**P- Reviewers:** Amiya E, Celikyurt YU, Davila DF, Hosoda T, Kolettis TM **S- Editor:** Wen LL **L- Editor**: A **E- Editor**: Wu HL

World Journal of Surgical Procedures

Online Submissions: http://www.wjgnet.com/esps/
bpgoffice@wjgnet.com
doi:10.5412/wjsp.v4.i1.9

*World J Surg Proced* 2014 March 28; 4(1): 9-12
ISSN 2219-2832 (online)


MINIREVIEWS

# Review of (acquired) incidental, rare and difficult tracheoesophageal fistula management

Jose Paulo Freire, Jose Crespo Mendes de Almeida

Jose Paulo Freire, Jose Crespo Mendes de Almeida, Department of General Surgery, Hospital de Santa Maria, 1649-035 Lisbon, Portugal
Author contributions: Freire JP and Mendes de Almeida JC contributed equally to this work, acquiring and analysing data, writing and reviewing the manuscript, and both approve the version to be published.
Correspondence to: Jose Paulo Freire, MD, Department of General Surgery, Hospital de Santa Maria, Avenida Professor Egas Moniz, 1649-035 Lisbon, Portugal. freire20@sapo.pt
Telephone: +351-21-7805002 Fax: +351-21-0405808
Received: October 29, 2013 Revised: December 24, 2013
Accepted: January 17, 2014
Published online: March 28, 2014

## Abstract

Acquired benign tracheoesophageal fistula is a rare condition and a difficult problem. The rarity and unpredictable presentation of this condition makes the design and setting of randomized prospective trials impossible. Guidelines on this matter are also difficult to establish. Based on a comprehensive evaluation of published literature and their experience, the authors review the etiology and best options for treatment, either surgical and non surgical, according to present knowledge.



**Key words:** Tracheoesophageal fistula; Esophageal stents; Tracheal stents; Surgical treatment

**Core tip:** Acquired nonmalignant tracheoesophageal fistula is a rare life-threatening condition. Several management approaches have been proposed, without a real consensual approach. The authors review the published literature and discuss the different options.

Freire JP, Mendes de Almeida JC. Review of (acquired) incidental, rare and difficult tracheoesophageal fistula management. *World J Surg Proced* 2014; 4(1): 9-12 Available from: URL: http://www.wjgnet.com/2219-2832/full/v4/i1/9.htm DOI: http://dx.doi.org/10.5412/wjsp.v4.i1.9

## INTRODUCTION

Acquired benign tracheoesophageal fistula (TEF) is a rare condition and a difficult problem that simultaneously compromises the respiratory and digestive functions. Morbidity is very high and, in untreated patients, mortality is probably close to one hundred percent. Similarly, treatment is also very difficult and published collective experience scarce. The rarity and unpredictable presentation of this condition makes the design and setting of randomized prospective trials impossible and is a limiting factor for the quality of information derived from the very few retrospective series published so far. Guidelines on this matter are also difficult to establish since the few published data differ significantly in issues like fistula etiology and location and the clinical expertise of surgeons (thoracic, general, ear, nose and throat) and gastroenterologists.

Therefore, for surgeons facing this difficult issue, a full and comprehensive evaluation of the literature should consider all the published data and the specificities of the information provided, such as the correct assessment of hospital resources, namely, the collective experience of a mandatory multidisciplinary approach. In such a difficult and rare condition, to reach a large and sound clinical experience is very challenging. At best, the concurrent experience in other clinical fields will hopefully provide the skills to deal with acquired benign tracheoesophageal fistulas. Due to the complexity of this condition, a clinical surgeon uncomfortable with the management of this disease should refer these patients to an experienced center.

## THE SURGICAL APPROACH

Five important papers published on this subject can be

identified[1-5], coming from experienced surgical groups with a sound reputation and experience and reporting clinical good outcomes. However, none of those groups were able to treat more than 75 patients and only over a long period of 30 to 35 years could those numbers be reached. Published scientific evidence is, at best, on the expert opinion range (level 3). Hilgenberg *et al*[1] were probably the first to publish a systematic review on this complication based in their personal experience with 20 patients. Lesions were caused by tracheal intubation (14), blunt trauma (3), orthopedic cervical spine procedures (2) and foreign body ingestion (1). Almost all of these lesions involved the proximal esophagus and the surgical approach relied on tracheal resection and anastomosis with either a direct suture of the esophageal perforation (16 patients) or an end to end reconstruction (3). Mortality reached 10% and fistula recurrence 5%. The most useful recommendations were the importance of preoperative mechanical ventilation weaning and the use of interposition of healthy muscular tissue buttressing the tracheal and esophageal suture lines.

Mathisen *et al*[2] reported their results in 1991 with a series of 38 patients treated for tracheoesophageal fistulas over a 16 year period, later completed with another 36 patients operated on from 1992 to 2010[3]. Interestingly in this series, the largest published until now, the etiology changed, with a decreasing incidence of post intubation injuries (71.1% to 47.2%) whilst other causes, like esophageal surgery and laryngectomy complications, increased in prevalence (5.3% to 27.8%). Reported fistulas were mostly located in the mid and upper trachea (61% and 36%). The majority (92%) were less than 3 cm long. Surgical approach was mostly cervical or cervical plus upper sternotomy. There was a clear trend change, from tracheal resection and anastomosis to direct and simple repair of the tracheal lesions, during the time span of this study, which the authors attributed to the increase of complications of esophageal and laryngeal surgery as the cause of tracheoesophageal fistulas. In this setting, compared with post intubation injury, the destruction of tracheal tissue was found less disruptive and more suitable for a conservative approach. Although mortality decreased from over 10% to 2.8% in the second period, fistula recurrence more than doubled, general complications remained the same, the number of patients requiring a tracheal procedure increased more than four fold, and the patients that were not able to recover oral intake were in excess of 17.1%, a five fold increase over the first time period. The authors established a relationship between these events and the minor tracheal lesions, TEF occurring after resection of the esophagus or larynx, and they considered that the later conditions were more challenging problems with a higher rate of fistula recurrence. They also reinforce the statement for the use of healthy muscular tissue to protect suture lines, underlining the importance of mechanical ventilation weaning before endeavouring tracheal reconstruction. For ventilator dependent patients, the authors emphasize the need for an adequate endotracheal tube cuff placement distal to the fistula opening. They also sustain the need for optimization of the overall medical condition prior to any definitive surgical approach, through placement of a feeding jejunostomy and a decompression gastrostomy, the removal of nasogastric feeding tubes (which adds further damage to tissues), and control of sepsis. They argue against the use of temporary or definitive esophageal stents because, in their opinion, they do not contribute to the treatment of established lesions and may also enlarge TEF, creating giant fistulas.

Another very interesting study comes from Italy with Baisi *et al*[4] reporting 31 patients operated on for tracheoesophageal fistulas over a period of 18 years. In this series, two thirds of the fistulas were caused by endotracheal intubation. The other significant cause was orthopedic cervical spine surgery (4 patients). Laryngeal surgery was not identified as a cause and esophageal surgery accounted with only one case of a Zenker's diverticulectomy as the primary procedure. Fistulas were all proximal in the trachea and surgical approach was mainly cervical. Again, they agree with previous authors on the need for weaning the patient from mechanical ventilation and obtaining an optimal general and medical condition with endoscopic percutaneous gastrostomy, feeding jejunostomy and sepsis control. In their experience, tracheal resection and reanastomosis was rarely needed since 26 patients were treated with tracheal and esophageal direct suture. This approach is contradictory to Mathisen's claim that post intubation lesions are more disruptive of tracheal tissue and more often require tracheal resection. These last authors also emphasize the need for muscular tissue interposition. Mortality was low, with only one reported death.

A very important series comes from the Mayo Clinic in Rochester, with Deschamps[5] presenting the results from a-30-year retrospective review including 35 patients. In this series, fistula etiology differs significantly from previous data, with most TEFs related to post-esophagectomy complications, while the post-intubation lesions accounted for less than 6% of the cases. Other important differences were the presence of trauma (17.1%), mediastinal tuberculosis (14.3%), radiation therapy (5.7%) and the *de novo* reported presence of an indwelling airway or esophageal stents as a cause for TEF (11.4%). All these etiologies were previously unreported. Not surprisingly, fistula location was more widely distributed, the majority being located distally in the carina (9) and main bronchus (14). This modified the surgical approach and strategy, with most patients being operated on through a thoracotomy or a thoracotomy plus a cervicotomy or laparotomy. In some patients, segmental bronchial resection was needed. The number of TEF requiring a multistaged repair was also important (7) and reoperations for complications (esophageal leak, bleeding, recurrence of TEF and tracheal dehiscence) reached almost 22.8%. Despite those figures, mortality was only 5.7% and 29 patients (82.9%) were able to return to an oral diet. Still, a great number of patients were treated with single stage division of the fistula and direct repair of both the tracheal and esophageal defect. These authors concur with previous

reports on the importance of buttressing the suture lines and weaning the patients from mechanical ventilation, although they do not equally emphasize these procedures, particularly in cases where tracheal resection and anastomosis is not needed.

Bartels *et al*[6] presented a report on tracheobronchial lesions (including 4 TEF) exclusively as morbidity of post esophageal resections. They were more frequent with the transthoracic approach than with the transmediastinal route and all cases were evident up to one month after the original operation. Prevalence was 3.9%. Factors closely related to the occurrence of those lesions were neoadjuvant radiotherapy, extensive thoracic linfadenectomy and dissection, as well as insufficiently drained local sepsis (mostly from anastomotic leaks). Despite this surgical group experience and expertise in Siewert's report, mortality averaged 33% and was correlated with the above risk factors. The authors found no positive contribution for fibrin glue or stents use and underscored the importance of weaning the patient from mechanical ventilation and of the use of buttressing of suture lines.

## THE CONSERVATIVE APPROACH

For many years, esophageal stenting has been used in the management of malignant and benign dysphagia and tracheoesophageal fistulas[7]. Tracheal[8] and combined (tracheal and esophageal) stenting[9-12] were also reported, including combined surgical and endoscopic approaches. The results from these studies are difficult to analyze due to the mixed nature of the pathologies involved (benign, malign, strictures, isolated esophageal or tracheal fistulas) and the diversity of stents used (plastic, metallic, covered or uncovered, retrievable or not). Major criticisms on this type of solutions for benign TEF are the low rate of fistula sealing without a real cure[13], the unnecessary and deleterious delay of definitive treatment and the potential for further damage of already traumatized tissue[14,15]. In fact, it is unlikely that the artificial surface of an esophageal prosthesis might allow, without the natural matrix provided by natural healthy tissue (muscle or other tissue buttressing), the healing of the *pars membranosa* of the trachea, the anterior wall of the native or interponate esophagus or both. This is mostly true in a patient dependent on mechanical ventilation because positive pressure will fuel the conditions for a perpetual tracheal leak. The same holds true for tracheal prosthesis alone. In this case, despite effective sealing of the airway, the esophageal leak will be responsible for local sepsis and persistent fistula. However, we found that a tracheal prosthesis that seals the airway defect might be temporarily useful, protecting the tracheal suture and tissue buttressing during unavoidable mechanical ventilation in the post operative period[8]. Its temporary and cautious use might also correct (modulate) late tracheal stenosis after surgical procedures. Recently, we used this approach with good results on a patient successfully operated on for TEF (post tracheal intubation) that subsequently developed isolated tracheal stenosis (unpublished data).

In our personal series, we also registered 2 TEF after esophageal resection for cancer (3.1% of the esophagectomies performed) with both patients submitted to neoadjuvant radiotherapy. Both patients were operated on through a thoracic approach and both suffered from long lasting cervical anastomotic leaks. The risk factors were identical to the ones reported in the Siewert[6] series but, in these cases, the TEF presented late, at 3 and 9 months after esophagectomy and cervical anastomotic leaks closure (unpublished data). A conservative approach was initially selected, with esophageal or tracheal prosthesis, but this approach failed and both patients were later operated on (tracheal and esophageal suture and sternocleidomastoid muscle interposition). One recovered uneventfully from the surgical procedure. The other patient suffered from recurrence of the fistula, reoperation, and finally, transsternal definitive tracheostomy followed by death from sepsis and multiple organ failure.

Finally, a 5$^{th}$ patient was operated on with a TEF resulting from a long lasting (1 year) tracheal stent initially inserted to treat a post intubation stenosis. This case underlines the indwelling esophageal or tracheal prosthesis risk of TEF.

## CONCLUSION

Treating benign TEF is challenging and a very difficult problem due to the potential devastating complications, patient suffering and death. Personal or institutional experience is scarce and even "high volume" centers face this problem at most once a year. There are no randomized studies or guidelines and only expert opinion is available[1-6,16]. Furthermore, published series differ significantly over important issues like fistula etiology and location, hospital resources and specificities of surgical and gastroenterology training. Therefore, for the occasional surgeon facing this problem, there are "off the shelf" solutions. Thus, these cases should be referred to experienced centers.

TEF patients require a multidisciplinary approach, encompassing the cooperation not only of surgical specialties (general, thoracic, ear, nose and throat), but also anesthesiologists and intensivists who in the end will have to manage and secure the airway in a complicated and difficult acute setting. This is a very important statement and only Baisi *et al*[4] report briefly and incompletely state this need. There are in fact a few studies published by anesthesiologists[17,18] reporting the difficulties they faced and the imaginative solutions that they used to overcome these uncommon situations. Some of these reports deserve to be carefully consulted, discussed and made available to all surgical teams as in some cases the reported "tricks" may make a substantial difference.

From the surgical point of view, some important issues are consensual. Almost all groups agree on the advantage of unsupported ventilation before any major surgical procedure. An optimal medical condition also should be pursued, namely through a gastric decompression and feeding jejunostomy tube placement. If at all

possible, the simpler surgical solution is certainly the best, that is, use of a single surgical approach (cervical or thoracic), a direct suture of the tracheal and esophageal lesions and the placement muscle interposition between suture lines. In fact, only Camargo *et al*[19] seems to minimize the importance of this simple, harmless and effective step. In spite of the complexity and etiology of TEF, a recent trend for less frequent tracheal resections, less frequent use of multistage procedures and esophageal exclusion or diversion is apparent.

Every surgeon must be prepared for complex and demanding procedures like tracheal resection and reconstruction, laryngotracheal resection and reconstruction eventually associated with major esophageal surgery.

The use of stents in benign situations must be cautious, temporary, tailored for specific situations, and should not be considered as a definitive approach. However, during the post operative period when a distal to the suture line tracheal tube placement is not possible, they may have a role as an adjunct, either as a short bridge for a definite surgical approach or as an airway protection procedure in a mechanical ventilation dependent patient.

## REFERENCES


1 **Hilgenberg AD**, Grillo HC. Acquired nonmalignant tracheoesophageal fistula. *J Thorac Cardiovasc Surg* 1983; **85**: 492-498 [PMID: 6834870]

2 **Mathisen DJ**, Grillo HC, Wain JC, Hilgenberg AD. Management of acquired nonmalignant tracheoesophageal fistula. *Ann Thorac Surg* 1991; **52**: 759-765 [PMID: 1929626 DOI: 10.1016/0003-4975(91)91207-C]

3 **Muniappan A**, Wain JC, Wright CD, Donahue DM, Gaissert H, Lanuti M, Mathisen DJ. Surgical treatment of nonmalignant tracheoesophageal fistula: a thirty-five year experience. *Ann Thorac Surg* 2013; **95**: 1141-1146 [PMID: 23000263 DOI: 10.1016/j.athoracsur.2012.07.041]

4 **Baisi A**, Bonavina L, Narne S, Peracchia A. Benign tracheoesophageal fistula: results of surgical therapy. *Dis Esophagus* 1999; **12**: 209-211 [PMID: 10631915 DOI: 10.1046/j.1442-2050.1999.00052.x]

5 **Shen KR**, Allen MS, Cassivi SD, Nichols FC, Wigle DA, Harmsen WS, Deschamps C. Surgical management of acquired nonmalignant tracheoesophageal and bronchoesophageal fistulae. *Ann Thorac Surg* 2010; **90**: 914-918; discussion 919 [PMID: 20732517 DOI: 10.1016/j.athoracsur.2010.05.061]

6 **Bartels HE**, Stein HJ, Siewert JR. Tracheobronchial lesions following oesophagectomy: prevalence, predisposing factors and outcome. *Br J Surg* 1998; **85**: 403-406 [PMID: 9529504 DOI: 10.1046/j.1365-2168.1998.00579.x]

7 **Adler DG**, Baron TH. Endoscopic palliation of malignant dysphagia. *Mayo Clin Proc* 2001; **76**: 731-738 [PMID: 11444406 DOI: 10.1016/S0025-6196(11)65004-0]

8 **Freire JP**, Feijó SM, Miranda L, Santos F, Castelo HB. Tracheo-esophageal fistula: combined surgical and endoscopic approach. *Dis Esophagus* 2006; **19**: 36-39 [PMID: 16364042 DOI: 10.1111/j.1442-2050.2006.00535.x]

9 **Ellul JP**, Morgan R, Gold D, Dussek J, Mason RC, Adam A. Parallel self-expanding covered metal stents in the trachea and oesophagus for the palliation of complex high tracheo-oesophageal fistula. *Br J Surg* 1996; **83**: 1767-1768 [PMID: 9038564 DOI: 10.1002/bjs.1800831233]

10 **Freitag L**, Tekolf E, Steveling H, Donovan TJ, Stamatis G. Management of malignant esophagotracheal fistulas with airway stenting and double stenting. *Chest* 1996; **110**: 1155-1160 [PMID: 8915213 DOI: 10.1378/chest.110.5.1155]

11 **Belleguic C**, Lena H, Briens E, Desrues B, Bretagne JF, Delaval P, Kernec J. Tracheobronchial stenting in patients with esophageal cancer involving the central airways. *Endoscopy* 1999; **31**: 232-236 [PMID: 10344427 DOI: 10.1055/s-1999-13674]

12 **van den Bongard HJ**, Boot H, Baas P, Taal BG. The role of parallel stent insertion in patients with esophagorespiratory fistulas. *Gastrointest Endosc* 2002; **55**: 110-115 [PMID: 11756930 DOI: 10.1067/mge.2002.119731]

13 **Blackmon SH**, Santora R, Schwarz P, Barroso A, Dunkin BJ. Utility of removable esophageal covered self-expanding metal stents for leak and fistula management. *Ann Thorac Surg* 2010; **89**: 931-936; discussion 936-937 [PMID: 20172156 DOI: 10.1016/j.athoracsur.2009.10.061]

14 **Eleftheriadis E**, Kotzampassi K. Temporary stenting of acquired benign tracheoesophageal fistulas in critically ill ventilated patients. *Surg Endosc* 2005; **19**: 811-815 [PMID: 15868255 DOI: 10.1007/s00464-004-9137-x]

15 **Han Y**, Liu K, Li X, Wang X, Zhou Y, Gu Z, Ma Q, Jiang T, Huang L, Zhang T, Cheng Q. Repair of massive stent-induced tracheoesophageal fistula. *J Thorac Cardiovasc Surg* 2009; **137**: 813-817 [PMID: 19327501 DOI: 10.1016/j.jtcvs.2008.07.050]

16 **Chauhan SS**, Long JD. Management of Tracheoesophageal Fistulas in Adults. *Curr Treat Options Gastroenterol* 2004; **7**: 31-40 [PMID: 14723836 DOI: 10.1007/s11938-004-0023-3]

17 **Malik AM**, Ahmed Z, Durgham N, Stockmann PT, Belenky WM, Zestos M. Airway and ventilation management during repair of a large acquired tracheoesophageal fistula: the novel use of a readily available tool. *J Clin Anesth* 2012; **24**: 133-136 [PMID: 22342211]

18 **Robins B**, Das AK. Anesthetic management of acquired tracheoesophageal fistula: a brief report. *Anesth Analg* 2001; **93**: 903-905; table of contents [PMID: 11574354]

19 **Camargo JJ**, Machuca TN, Camargo SM, Lobato VF, Medina CR. Surgical treatment of benign tracheo-oesophageal fistulas with tracheal resection and oesophageal primary closure: is the muscle flap really necessary? *Eur J Cardiothorac Surg* 2010; **37**: 576-580 [PMID: 19800809 DOI: 10.1016/j.ejcts.2009.08.023]


**P- Reviewers:** Ferri A, Stefano C, Thomas S **S- Editor:** Song XX
**L- Editor:** Roemmele A **E- Editor**: Wu HL

World Journal of Surgical Procedures

Online Submissions: http://www.wjgnet.com/esps/
bpgoffice@wjgnet.com
doi:10.5412/wjsp.v4.i1.13

*World J Surg Proced* 2014 March 28; 4(1): 13-20
ISSN 2219-2832 (online)


MINIREVIEWS

# Diagnostic imaging and interventional procedures in a growing problem: Hepatic alveolar echinococcosis

Mecit Kantarci, Berhan Pirimoglu, Yesim Kizrak

Mecit Kantarci, Berhan Pirimoglu, Yesim Kizrak, Department of Radiology, School of Medicine, Ataturk University, 25090 Erzurum, Turkey
Author contributions: Kantarci M and Pirimoglu B designed the research; Kantarci M, Pirimoglu B and Kizrak Y performed the research; Kantarci M and Kızrak Y analyzed the data; Kantarci M and Pirimoglu B wrote the paper.
Correspondence to: Mecit Kantarci, MD, PhD, Department of Radiology, School of Medicine, Ataturk University, 200 Evler Mah. 14. Sok No 5 Dadaskent, 25090 Erzurum, Turkey. akkanrad@hotmail.com
Telephone: +90-442-2361212 Fax: +90-442-2361301
Received: October 28, 2013 Revised: December 19, 2013
Accepted: February 16, 2014
Published online: March 28, 2014

## Abstract

Alveolar echinococcosis (AE) of the liver is caused by the metacestode of the fox tapeworm *Echinococcus multilocularis* (*E. multilocularis*), which is endemic in many parts of the world. AE is a very aggressive and potentially fatal infestation which always affects the liver primarily and metastasizes to any part of the body. Without timely diagnosis and therapy, the prognosis is dismal, with death the eventual outcome in most cases. Diagnosis is usually based on findings at radiological imaging and in serological analyses. The alveolar cysts grow by exogenous proliferation and behave like a malignant neoplasm. Since AE lesions can occur almost anywhere in the body, familiarity with the spectrum of cross-sectional imaging appearances is advantageous. Therefore, AE lesions can cause physicians to generate a long list of differential diagnoses, including malignant tumors. Disseminated parasitic lesions in unusual locations with atypical imaging appearances may make it difficult to narrow the differential diagnosis. For diagnosis, ultrasonography (US) remains the first line examination. For a more accurate disease evaluation, aiming to guide the surgical strategy, computed tomography (CT), magnetic resonance imaging (MRI), including magnetic resonance cholangiography (MRC) imaging, are of importance, providing useful complementary information. However, making the correct diagnosis is possible if imaging findings are correlated with appropriate clinical findings. We present an overview of the radiological patterns produced by *E. multilocularis* lesions as seen on US, CT and MRI and discuss the interventional procedures in hepatic AE lesions.



**Key words:** Alveolar echinococcosis; Liver; Diagnosis; Intervention; Imaging; Review

**Core tip:** Diagnosis and treatment of alveolar echinococcosis remains a challenge for clinicians. Most patients suffering from a chronic carrier status need continuous medical treatment and follow-up examinations. Diagnosis of alveolar echinococcosis is supported by results from imaging studies, histopathology and/or serological analyses. The present review summarizes current understanding of imaging features and knowledge of interventional procedures.

Kantarci M, Pirimoglu B, Kizrak Y. Diagnostic imaging and interventional procedures in a growing problem: Hepatic alveolar echinococcosis. *World J Surg Proced* 2014; 4(1): 13-20 Available from: URL: http://www.wjgnet.com/2219-2832/full/v4/i1/13.htm DOI: http://dx.doi.org/10.5412/wjsp.v4.i1.13

## INTRODUCTION

Alveolar echinococcosis (AE) is a rare parasitic disease due to the intra-hepatic development of the larva of the small metacestode *Echinococcus multilocularis* (*E. multilocularis*). Metacestode cells of *E. multilocularis* proliferate in the liver, inducing slowly progressive, life-threatening tumor like growths[1,2]. The prognosis is generally poor

and liver transplantation may be required in patients with inoperable lesions, chronic liver failure[2,3]. Most patients suffering from a chronic carrier status need continuous medical treatment and follow-up examinations[1,4]. In addition to anti-infective therapy with benzimidazoles, early diagnosis by imaging techniques, radical surgery, transplantation, radiological interventional procedures and long term medical care of the patients have contributed to the success of treatment and increase in patient survival time[5].

This article provides an epidemiological, pathophysiological, diagnostic profile of the disease as background for a detailed review of the clinical, interventional approach, and radiological features of hepatic AE. The current roles of specific imaging modalities are described to aid radiologists in the timely detection and characterization of AE infestations.

## EPIDEMIOLOGICAL AND PATHOPHYSIOLOGICAL CHARACTERISTICS

Most human cases of *E. multilocularis* infection have been reported in endemic areas of western and central Europe, including Turkey, the former Soviet Union, Iran, Iraq, western and central China, and northern Japan[6]. Definitive hosts are foxes and, less commonly, cats and dogs. Intermediate hosts are wild rodents. Humans are infested either by direct contact with definitive hosts or indirectly by intake of contaminated water or contaminated plants, such as wild berries[6,7]. Humans are accidental intermediate hosts, becoming infected after ingesting contaminated foods, including fruits and vegetables[8]. The walls of the parasite eggs are destroyed in the host digestive system, after which the embryos penetrate the intestinal wall and reach the liver, by way of the portal or lymphatic system, where the larvae develop. In the liver, *E. multilocularis* larvae grow as tumor-like buds that evolve into multiple vesicles containing a germinal layer surrounded by a laminar membrane[4]. The liver parenchyma near the mass is typically atrophic with capsular retraction due to biliary or vascular invasion. Necrosis is observed in the center of the lesions; moreover, these lesions may become superinfected with bacteria and fungi, possibly leading to complications such as liver abscesses and septicemia. The larva causes invasive and destructive changes in the human host that often lead to complications[7-9].

Hepatic AE is a chronic disease with a latent stage that may last for years before signs and symptoms develop. If left untreated, the disease is usually fatal. Death eventually results from hepatobiliary complications, such as biliary obstruction with bacterial or fungal superinfection or secondary biliary cirrhosis, bleeding from esophageal or duodenal varices due to portal hypertension, Budd-Chiari disease or obstruction of the vena cava[9,10].

## CLINICAL FEATURES

The liver is the most common site of *E. multilocularis* infection, with more than 90% of patients having infected livers. The lesions may be single or multiple[4]. Alveolar echinococcosis of the liver behaves like a slow growing liver cancer. Symptoms of hepatic alveolar echinococcosis are principally cholestatic jaundice and epigastric pain[3,7]. Involvement of the bile ducts and blood vessels leads to severe complications, such as cholangitis, portal hypertension, liver abscesses, septic shock and Budd-Chiari syndrome[11].

## DIAGNOSIS

Clinical diagnosis of hepatic AE is based on the patient's medical history, clinical features, morphological characteristics of lesions, determined at radiological imaging, and results of serological and histopathological analyses[7,8,12]. A diagnosis of alveolar echinococcosis is based on the presence of at least two of the following findings[4,12]: (1) a lesion or lesions with the typical appearance, detected in the usual sites at cross-sectional imaging; (2) echinococcus species-specific serum antibodies detected in blood tests with high diagnostic sensitivity and confirmed in immunoassays with high specificity; and (3) histopathological features suggestive of *E. multilocularis* and nucleic acid of *E. multilocularis* detected in a clinical specimen.

The World Health Organization Informal Working Group on Echinococcosis classification system, based on imaging findings, has been established as the international benchmark for standardized evaluation of diagnostic and therapeutic measures[13]. This PNM-system denotes the extension of the primary mass in the liver (P), the involvement of neighboring organs including lymph nodes (N), and metastases (M)[14] (Table 1).

## IMAGING METHODS FOR DETECTING THE HEPATIC AE LESIONS

Abdominal ultrasonography (US) is the first line imaging examination for evaluation of patients in whom the presence of alveolar echinococcosis is suspected. Computed tomography (CT) and magnetic resonance (MR) imaging performed with cholangiopancreatography and diffusion-weighted techniques, as well as standard sequences, typically are required for preoperative evaluation[4,8,10]. Recently, we have performed CT perfusion imaging for demonstration of the perfusion characteristics of the hepatic AE lesions and to make a differential diagnosis between AE and other malignant liver lesions.

### *US*

US is the initial investigative modality of choice for detection of hepatic AE lesions[4,12]. Typical findings at abdominal US (in approximately 70% of cases) include a large hepatic mass with juxtaposed areas of internal hyper- and hypo-echoic, irregular margins and scattered foci of calcification, and a pseudocyst with a large area of central necrosis surrounded by an irregular ring like region of hyperechoic representing fibrous tissue[15] (Figure 1A).

**Table 1 PNM classification of alveolar echinococcosis**

| | |
|---|---|
| P | Primary lesion localized to the liver |
| PX | Primary lesion cannot be assessed |
| P0 | No detectable hepatic lesion |
| P1 | Peripheral hepatic lesion with no proximal hepatic vascular or biliary involvement |
| P2 | Central hepatic lesion with proximal involvement of vessels or biliary ducts in one lobe[1] |
| P3 | Central hepatic lesion with involvement of hilar vessels or biliary ducts in both lobes or with involvement of two hepatic veins |
| P4 | Hepatic lesion with extension along the vessels[2] and biliary tree |
| N | Extrahepatic involvement of neighboring organs or tissues [diaphragm, lung, pleura, pericardium, heart, gastric or duodenal wall, adrenal gland, peritoneum, retroperitoneum, parietal wall (muscles, skin, bone), pancreas, regional lymph nodes, hepatic ligaments, kidney] |
| NX | Cannot be evaluated |
| N0 | No regional involvement |
| N1 | Regional involvement of contiguous organs or tissues |
| M | Absence or presence of distant metastasis (in lung, distant lymph nodes, spleen, central nervous system, orbits, bone, skin, muscle, kidney, distant peritoneum, and retroperitoneum) |
| MX | Not completely evaluated |
| M0 | No metastasis[3] |
| M1 | Metastasis |

[1]For purposes of PNM classification, the liver is considered to be divided into two lobes by a plane projecting between the gallbladder bed and the inferior vena cava; [2]Vessels include the inferior vena cava, portal vein and arteries; [3]Absence of metastases is considered to be indicated by negative findings at chest radiography and computed tomography of the brain.

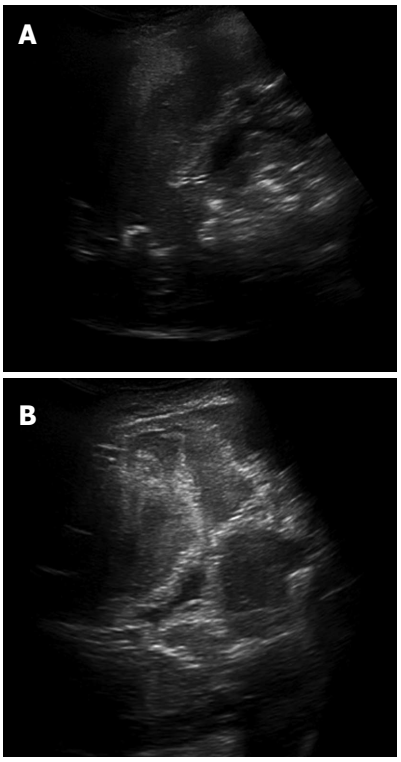


**Figure 1 Alveolar echinococcosis in a 41-year-old woman.** Abdominal gray-scale ultrasonography (US) image shows a heterogeneous mass lesion in the right lobe of the liver. The mass is generally hypoechoic but contains hyperechoic foci of calcifications (A). Alveolar echinococcosis in a 38 year old woman. Abdominal gray-scale US image shows a heterogeneous, hyperechoic lesion without calcifications (B).

Less typical appearances (in approximately 30% of cases) include multiple clustered hemangioma-like hyperechoic nodules (Figure 1B). These lesions usually show a "hail-storm pattern". This pattern represents the histopathologically heterogeneous stroma containing microscopic metacestode vesicles, areas of non liquefactive necrosis, entrapped host tissue and microcalcifications, which account for the stroma's relatively increased echogenicity[16]. Irregular borders and a lack of enhancement are suggestive of AE; the other liver lesions usually enhance and are rarely calcified. A pseudocyst appearance might also be seen in recurrent foci of AE after percutaneous drainage of primary lesions[11,16]. Doppler US images can show distortion and displacement of the hepatic veins, portal vein and biliary tree resulting from mass effect, invasion of the inferior vena cava, hepatic or portal vein walls, and intrahepatic bile duct dilatation[8].

### CT

CT reveals anatomical and morphological features of lesions and best detects the characteristic pattern of calcification. It also allows to help determine the number, size and location of lesions in the liver and allows a comprehensive preoperative evaluation of vascular, biliary and extrahepatic extension, which is an important consideration when assessing lesion resectability[4,16,17]. Non-contrast enhanced CT images show an infiltrating tumor like hepatic mass with irregular margins and heterogeneous contents with varied attenuation, including scattered hyperattenuating calcifications and hypoattenuation areas corresponding to necrosis and parasitic tissue (Figure 2A); these findings are characteristic findings of alveolar echinococcosis (18). Calcifications are found approximately in 90% of all infected patients. Apart from the typical peripheral irregular calcifications, large homogeneous, multiple punctiform or scattered calcifications might be seen[4,8,9,16].

Large areas of central necrosis can be difficult to differentiate from abscesses. However, there is poor or no enhancement after bolus administration of intravenous contrast agent, emphasizing poor vascularization of the parasitic lesion (Figure 2B). Usually, no lymphadenopathy occurs[18,19]. Secondary pyogenic infection may occur at any time during the course of disease, resulting in abscess formation. Hilar infiltration occurs in approximately 50% of all patients, resulting in dilatation of the intrahepatic bile ducts and invasion of the portal vein, the portal branches and the hepatic veins. These conditions lead to hypoperfusion and subsequent atrophy of the affected liver segments[4,8,19]. CT findings of the hepatic AE lesions may be indistinguishable from primary hepatic neoplasms, such as cholangiocarcinoma, biliary cystadenoma and biliary cystadenocarcinoma, as well as hepatic metastases[4,9,20]. However, hypoattenuation, calcification and absence of contrast enhancement in a hepatic lesion can help identify it as hepatic AE.

CT perfusion, a non-invasive method that has been increasingly used in recent years, allows for functional

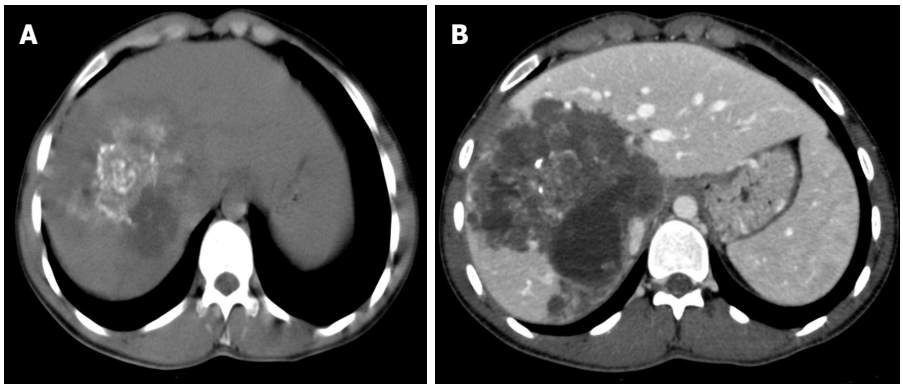


**Figure 2 Alveolar echinococcosis in a 34-year-old man.** Axial unenhanced computed tomography (CT) image demonstrates an infiltrating tumor-like hepatic mass with irregular margins and heterogeneous contents, including scattered hyperattenuating foci of calcification and areas of hypoattenuation corresponding to necrosis and parasite tissue (A). Alveolar echinococcosis in a 29 year old man. Abdominal CT images obtained after the administration of intravenous contrast medium show a poor enhancement, hypoattenuating lesion in the portal venous phase (B).

assessment of the perfusion of normal and pathological tissues by means of parameters such as the blood flow (BF), blood volume (BV), mean transit time (MTT), arterial liver perfusion (ALP), portal liver perfusion (PLP) and hepatic perfusion index (HPI). This technique allows for quantitative determination of lesion characteristics, enabling differentiation between malignant lesions and benign ones. Many studies have reported the use of this method to assess hepatocellular carcinoma, cirrhotic nodules and normal liver parenchyma[21]. Our experience suggests that CT perfusion is a feasible method to quantitatively assess angiogenesis of AE lesions of liver. We determined lower BF, BV, ALP and PVP values in AE lesions compared with normal liver parenchyma by using CT perfusion imaging (Figure 3). The above results demonstrated that CT perfusion can be used in hepatic AE lesions of liver that are confusable, especially with malignant lesions such as hepatocellular and cholangiocellular carcinoma.

### *MRI*

MRI is a good modality for detection of the components of parasitic lesions and depicting vascular or biliary tree involvement and extrahepatic extension. Therefore, it should be added to preoperative evaluations, particularly evaluations of patients who are to undergo extensive hepatic resection or liver transplantation[8]. MRC has been used to detect the relationship between hepatic AE lesions and the biliary tree before surgical treatment or liver transplantation[4]. However, non-contrast enhanced CT imaging is superior to MRI in detecting calcifications. The MRI characteristics are a heterogeneous infiltrative mass with irregular margins and a necrotic center that exhibits low to intermediate signal intensity on T1-weighted images and heterogeneous signal intensity (areas of low and high signal intensity) on T2-weighted images. Areas of high T2 signal intensity correspond to small cystic or necrotic components, whereas areas of low T2 signal intensity correspond to fibrotic or collagenous components (Figure 4). T2-weighted images are useful for detecting small hepatic cysts and extrahepatic cysts[22,23].

Hepatic AE lesions are categorized on the basis of their imaging manifestations into five types. Type 1 (4%) lesions consist of multiple small cysts without a solid tissue component; type 2 (40%) lesions include a solid tissue component associated with multiple small cysts; type 3 (46%) lesions consist of a solid tissue component associated with irregular large cysts; type 4 (4%) lesions consist of solid tissue without cystic components; and type 5 (6%) lesions consist of a single large cyst without solid tissue components[22]. For lesions with characteristics not often seen in AE (especially types 1, 4 and 5), serological analyses can be helpful[8]. In particular, MRC can detect biliary dilatation, a reduced number of bile ducts within the lesion, invasion of the biliary wall, distortion and compression of the biliary tree, and communication of intrahepatic bile ducts with necrotic cystic regions[8,23].

Signal intensity at diffusion-weighted imaging can be quantified by calculating the apparent diffusion coefficient (ADC), a valuable indicator for the diagnosis and characterization of focal hepatic lesions[24]. Our experience suggests that AE lesions can be reliably identified on diffusion-weighted images obtained with *b* values of 50400800 and 1000 sec/mm$^2$ and qualitatively assessed on ADC maps. These lesions usually result in a subjectively higher ADC in the lesion than in liver parenchyma on diffusion-weighted images obtained with a *b* value of 800 sec/mm$^2$ (Figure 5). Restricted diffusion due to a superinfection (especially an abscess) may be observed in the necrotic central part of particularly large AE lesions. The general lack of diffusion restriction in hepatic AE lesions is an important finding that helps differentiate them from malignancies that have similar clinical features and imaging findings, including invasion and metastases. Table 2 summarizes characteristic imaging features that are helpful for diagnosing hepatic AE lesions.

## INTERVENTIONAL PROCEDURES

In hepatic AE, radical surgical excision is followed by short-term antihelmintic therapy for resectable lesions and long-term aggressive antihelmintic therapy for par-

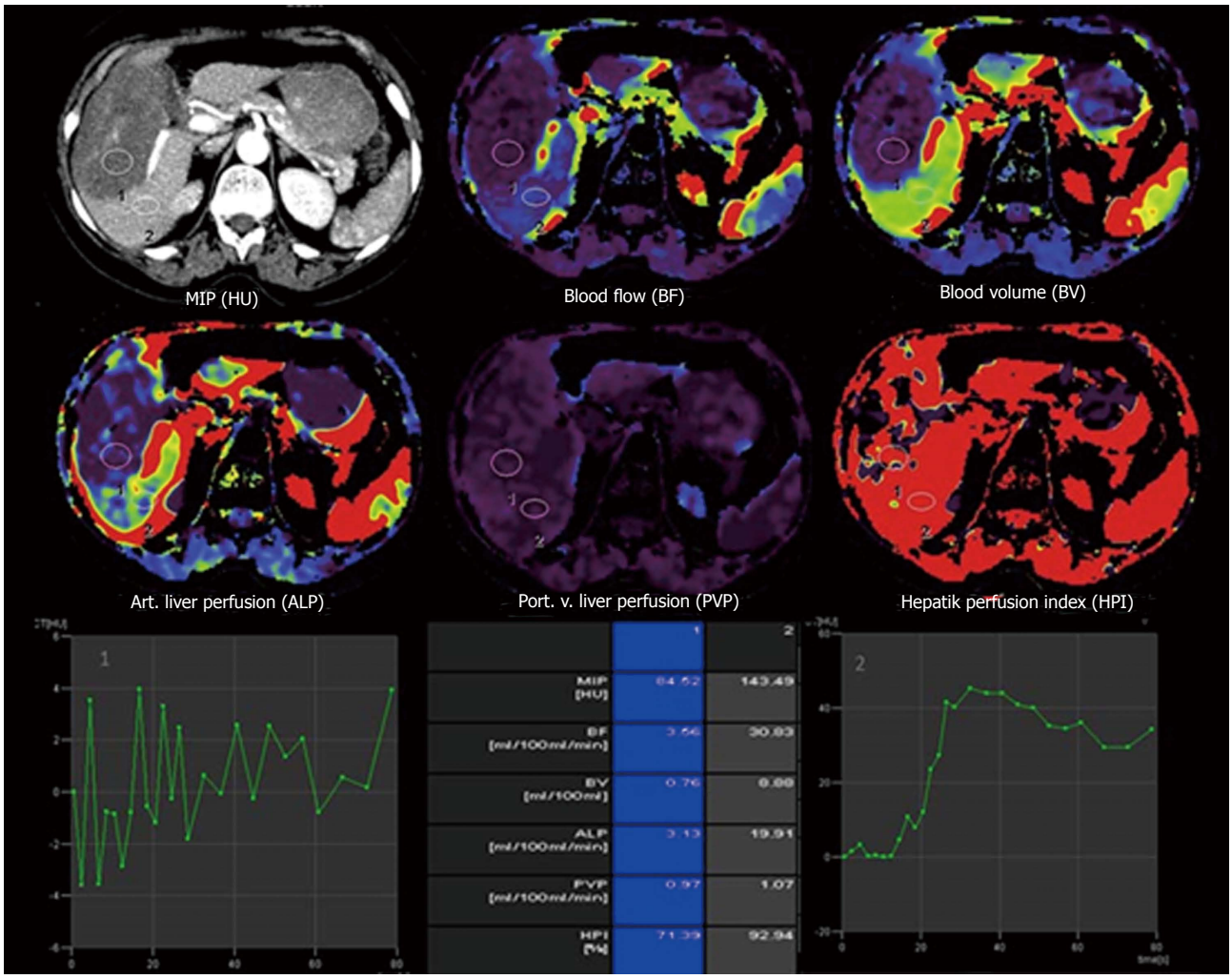


**Figure 3 Transverse computed tomography perfusion functional maps of the blood volume, blood flow, portal-venous perfusion, arterial liver perfusion and hepatic perfusion index in a 49-year-old woman show a large alveolar echinococcosis lesion in the right lobe of the liver that has a distinct range of colors compared with the background liver parenchyma.** Perfusion values from an ROI drawn in the solid component without calcification of alveolar echinococcosis (ROI 1) and normal tissue (ROI 2) show lower blood flow, blood volume, arterial liver perfusion and portal-venous perfusion values compared with normal liver parenchyma.

**Table 2 Morphological characteristics of hepatic alveolar echinococcosis lesions**

| Modality | Hepatic AE lesions |
|---|---|
| US | Mass with irregular margins, scattered foci of calcification, central necrosis, and vascular and biliary involvement |
| CT | |
| Unenhanced | Mass with irregular margins, hyperattenuating foci of calcification, and hypoattenuating regions of necrosis and parasitic tissue |
| Contrast- enhanced | Mass with no substantial enhancement and peripheral fibroinflammatory components with slight but long-lasting enhancement |
| CT perfusion | Lower BF, BV, ALP and PVP values in AE lesions compared with normal liver parenchyma |
| MRI | |
| T1-weighted | Heterogeneous mass with irregular margins and a necrotic center that exhibits low to intermediate signal intensity |
| T2-weighted | Heterogeneous mass with irregular margins, a necrotic center that exhibits high signal intensity, and low-signal-intensity fibrotic and collagenous components |
| Contrast-enhanced | Mass with no substantial enhancement and peripheral fibroinflammatory components with slight but long-lasting enhancement |
| Diffusion-weighted | Mass with hypointense signal and high ADC on images obtained with high *b* values |

AE: Alveolar echinococcosis; CT: Computed tomography; US: Ultrasonography; BF: Blood flow; BV: Blood volume; ALP: Arterial liver perfusion; PVP: Portal-venous perfusion; ADC: Apparent diffusion coefficient.

tially resectable or unresectable lesions. Patients with hepatic AE have a poor prognosis and high fatality rate; curative treatment of AE is possible only with early detection and complete surgical excision or liver transplantation[7,11]. Liver transplantation should only be considered in patients with very severe hilar extension, leading

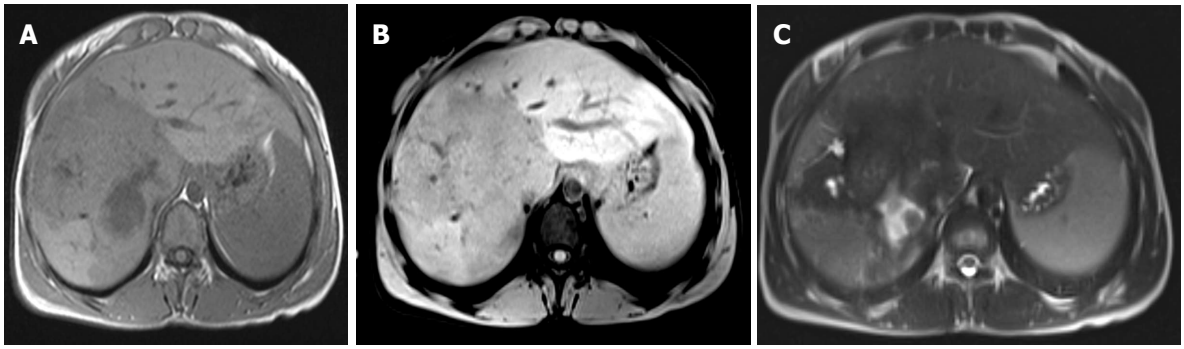


**Figure 4 Alveolar echinococcosis in a 39-year-old man.** Axial unenhanced T1-weighted image show an infiltrating hypointense mass in the right lobe of the liver (A). Axial magnetic resonance imaging obtained after the administration of intravenous contrast medium show no contrast enhancement within the mass (B). Axial T2-weighted image show an infiltrating hypointense mass in the right lobe of the liver (C).

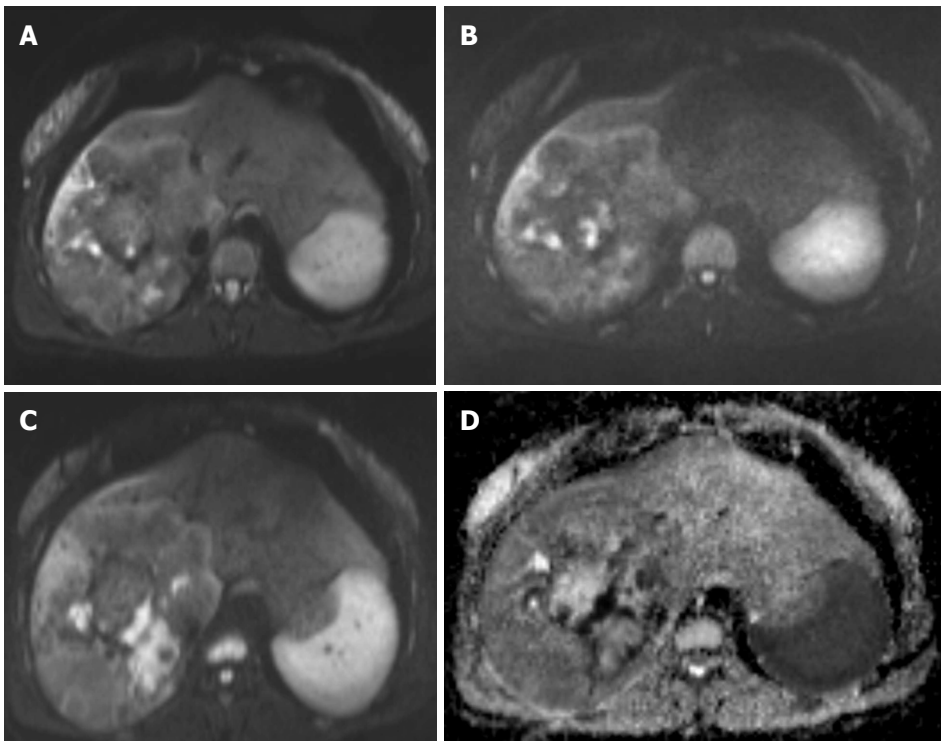


**Figure 5 Alveolar echinococcosis in a 44-year-old man.** Diffusion-weighted magnetic resonance images obtained with *b* values of 400 sec/mm$^2$ (A), 800 sec/mm$^2$ (B), and 1000 sec/mm$^2$ (C) and corresponding apparent diffusion coefficient map (D) show signal hyperintensity in a hepatic mass.

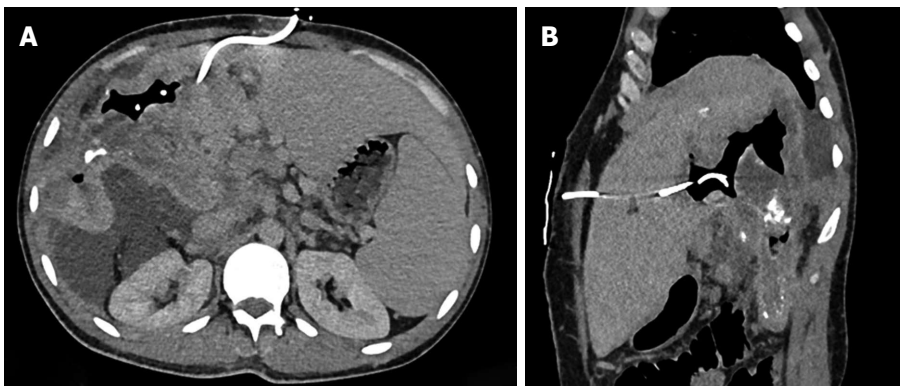


**Figure 6 Non-contrast enhanced axial (A) and sagittal (B) computed tomography images show the percutaneous drainage of an infected parasitic cyst in a 43 year old woman with hepatic alveolar echinococcosis.**

to uncontrolled biliary infections, symptomatic secondary biliary cirrhosis with ascites and/or severe variceal bleeding owing to portal hypertension[25].

Cases of late diagnosis require lifelong pharmacological treatment with benzimidazoles and thorough follow-up because benzimidazoles are assumed to exert only a parasitostatic effect on hepatic AE lesions. Albendazole is a broad spectrum anthelmintic agent. Perioperative treatment with albendazole can decrease the recurrence rate and increase the success rate of the operation[17,26]. Management of the septic complications of alveolar echinococcosis of the liver, such as cholangitis or liver abscesses, should prioritize interventional radiology[4,25]. The liver abscess is usually treated by percutaneous catheterization, which may lead to complete disappearance of the hepatic alveolar echinococcus lesion[11] (Figure 6). Additionally, treatment of portal hypertension in alveolar echinococcosis of the liver is also problematic. In patients without cirrhosis, percutaneous stent placement in the hepatic veins is a promising treatment alternative[27].

## CONCLUSION

Hepatic AE lesions mimic slow-growing tumors of the liver parenchyma that tend to infiltrate adjacent structures, especially the portal hilum, hepatic veins, inferior vena cava and biliary system. For effective service to referring clinicians and their patients, radiologists should be familiar with the cross-sectional imaging findings of hepatic AE. Therefore, radiologists should depict in detail the relationships between the mass and the portal bifurcation, especially any evidence of invasion or extension into the main portal vein, hepatic veins, inferior vena cava and bile ducts. Additionally, if liver transplantation is contemplated, the remaining functional hepatic parenchymal mass and reserve should be calculated and septic complications should be treated by percutaneous drainage until performing the radical surgical excision or liver transplantation.

## REFERENCES


1 **Craig P**. Echinococcus multilocularis. *Curr Opin Infect Dis* 2003; **16**: 437-444 [PMID: 14501996 DOI: 10.1097/00001432-200310000-00010]

2 **Kern P**, Bardonnet K, Renner E, Auer H, Pawlowski Z, Ammann RW, Vuitton DA, Kern P. European echinococcosis registry: human alveolar echinococcosis, Europe, 1982-2000. *Emerg Infect Dis* 2003; **9**: 343-349 [PMID: 12643830 DOI: 10.3201/0903.020341]

3 **Koch S**, Bresson-Hadni S, Miguet JP, Crumbach JP, Gillet M, Mantion GA, Heyd B, Vuitton DA, Minello A, Kurtz S. Experience of liver transplantation for incurable alveolar echinococcosis: a 45-case European collaborative report. *Transplantation* 2003; **75**: 856-863 [PMID: 12660515 DOI: 10.1097/01.TP.0000054230.63568.79]

4 **Kantarci M**, Bayraktutan U, Karabulut N, Aydinli B, Ogul H, Yuce I, Calik M, Eren S, Atamanalp SS, Oto A. Alveolar echinococcosis: spectrum of findings at cross-sectional imaging. *Radiographics* 2012; **32**: 2053-2070 [PMID: 23150858 DOI: 10.1148/rg.327125708]

5 **Torgerson PR**, Schweiger A, Deplazes P, Pohar M, Reichen J, Ammann RW, Tarr PE, Halkik N, Müllhaupt B. Alveolar echinococcosis: from a deadly disease to a well-controlled infection. Relative survival and economic analysis in Switzerland over the last 35 years. *J Hepatol* 2008; **49**: 72-77 [PMID: 18485517 DOI: 10.1016/j.jhep.2008.03.023]

6 **Vuitton DA**, Zhou H, Bresson-Hadni S, Wang Q, Piarroux M, Raoul F, Giraudoux P. Epidemiology of alveolar echinococcosis with particular reference to China and Europe. *Parasitology* 2003; **127** Suppl: S87-107 [PMID: 15027607 DOI: 10.1017/S0031182003004153]

7 **McManus DP**, Zhang W, Li J, Bartley PB. Echinococcosis. *Lancet* 2003; **362**: 1295-1304 [PMID: 14575976 DOI: 10.1016/S0140-6736(03)14573-4]

8 **Bresson-Hadni S**, Delabrousse E, Blagosklonov O, Bartholomot B, Koch S, Miguet JP, André Mantion G, Angèle Vuitton D. Imaging aspects and non-surgical interventional treatment in human alveolar echinococcosis. *Parasitol Int* 2006; **55** Suppl: S267-S272 [PMID: 16403670 DOI: 10.1016/j.parint.2005.11.053]

9 **Czermak BV**, Unsinn KM, Gotwald T, Waldenberger P, Freund MC, Bale RJ, Vogel W, Jaschke WR. Echinococcus multilocularis revisited. *AJR Am J Roentgenol* 2001; **176**: 1207-1212 [PMID: 11312183 DOI: 10.2214/ajr.176.5.1761207]

10 **Polat K**, Ozturk G, Aydinli B, Kantarci M. Images of interest. Hepatobiliary and pancreatic: alveolar hydatid disease. *J Gastroenterol Hepatol* 2004; **19**: 1319 [PMID: 15482542 DOI: 10.1111/j.1440-1746.2004.03629]

11 **Koroglu M**, Akhan O, Gelen MT, Koroglu BK, Yildiz H, Kerman G, Oyar O. Complete resolution of an alveolar echinococcosis liver lesion following percutaneous treatment. *Cardiovasc Intervent Radiol* 2006; **29**: 473-478 [PMID: 16228851 DOI: 10.1007/s00270-005-0017-0]

12 **Kern P**. Clinical features and treatment of alveolar echinococcosis. *Curr Opin Infect Dis* 2010; **23**: 505-512 [PMID: 20683265 DOI: 10.1097/QCO.0b013e32833d7516]

13 Guidelines for treatment of cystic and alveolar echinococcosis in humans. WHO Informal Working Group on Echinococcosis. *Bull World Health Organ* 1996; **74**: 231-242 [PMID: 8789923]

14 **Li T**, Chen X, Zhen R, Qiu J, Qiu D, Xiao N, Ito A, Wang H, Giraudoux P, Sako Y, Nakao M, Craig PS. Widespread coendemicity of human cystic and alveolar echinococcosis on the eastern Tibetan Plateau, northwest Sichuan/southeast Qinghai, China. *Acta Trop* 2010; **113**: 248-256 [PMID: 19941830 DOI: 10.1016/j.actatropica.2009.11.006]

15 **Bartholomot G**, Vuitton DA, Harraga S, Shi DZ, Giraudoux P, Barnish G, Wang YH, MacPherson CN, Craig PS. Combined ultrasound and serologic screening for hepatic alveolar echinococcosis in central China. *Am J Trop Med Hyg* 2002; **66**: 23-29 [PMID: 12135263]

16 **Choji K**, Fujita N, Chen M, Spiers AS, Morita Y, Shinohara M, Nojima T, Irie G. Alveolar hydatid disease of the liver: computed tomography and transabdominal ultrasound with histopathological correlation. *Clin Radiol* 1992; **46**: 97-103 [PMID: 1395417 DOI: 10.1016/S0009-9260(05)80311-3]

17 **Reuter S**, Nüssle K, Kolokythas O, Haug U, Rieber A, Kern P, Kratzer W. Alveolar liver echinococcosis: a comparative study of three imaging techniques. *Infection* 2001; **29**: 119-125 [PMID: 11440381 DOI: 10.1007/s15010-001-1081-2]

18 **Karçaaltincaba M**, Sirlin CB. CT and MRI of diffuse lobar involvement pattern in liver pathology. *Diagn Interv Radiol* 2011; **17**: 334-342 [PMID: 21053176 DOI: 10.4261/1305-3825.DIR.4033-10.0]

19 **Akin O**, Isiklar I. Hepatic alveolar echinococcosis. A case report. *Acta Radiol* 1999; **40**: 326-328 [PMID: 10335973 DOI: 10.3109/02841859909175562]

20 **Didier D**, Weiler S, Rohmer P, Lassegue A, Deschamps JP, Vuitton D, Miguet JP, Weill F. Hepatic alveolar echinococcosis: correlative US and CT study. *Radiology* 1985; **154**: 179-186 [PMID: 3880602]

21 **Ippolito D**, Bonaffini PA, Capraro C, Leni D, Corso R, Sironi

S. Viable residual tumor tissue after radiofrequency ablation treatment in hepatocellular carcinoma: evaluation with CT perfusion. *Abdom Imaging* 2013; **38**: 502-510 [PMID: 22743839 DOI: 10.1007/s00261-012-9924-0]

22 **Kodama Y**, Fujita N, Shimizu T, Endo H, Nambu T, Sato N, Todo S, Miyasaka K. Alveolar echinococcosis: MR findings in the liver. *Radiology* 2003; **228**: 172-177 [PMID: 12750459 DOI: 10.1148/radiol.2281020323]

23 **Balci NC**, Tunaci A, Semelka RC, Tunaci M, Ozden I, Rozanes I, Acunas B. Hepatic alveolar echinococcosis: MRI findings. *Magn Reson Imaging* 2000; **18**: 537-541 [PMID: 10913715 DOI: 10.1016/S0730-725X(00)00145-4]

24 **Koh DM**, Scurr E, Collins DJ, Pirgon A, Kanber B, Karanjia N, Brown G, Leach MO, Husband JE. Colorectal hepatic metastases: quantitative measurements using single-shot echo-planar diffusion-weighted MR imaging. *Eur Radiol* 2006; **16**: 1898-1905 [PMID: 16691378 DOI: 10.1007/s00330-006-0201-x]

25 **Bresson-Hadni S**, Koch S, Miguet JP, Gillet M, Mantion GA, Heyd B, Vuitton DA. Indications and results of liver transplantation for Echinococcus alveolar infection: an overview. *Langenbecks Arch Surg* 2003; **388**: 231-238 [PMID: 12905036 DOI: 10.1007/s00423-003-0394-2]

26 **Reuter S**, Buck A, Manfras B, Kratzer W, Seitz HM, Darge K, Reske SN, Kern P. Structured treatment interruption in patients with alveolar echinococcosis. *Hepatology* 2004; **39**: 509-517 [PMID: 14768005 DOI: 10.1002/hep.20078]

27 **Vogel J**, Görich J, Kramme E, Merkle E, Sokiranski R, Kern P, Brambs HJ. Alveolar echinococcosis of the liver: percutaneous stent therapy in Budd-Chiari syndrome. *Gut* 1996; **39**: 762-764 [PMID: 9026484 DOI: 10.1136/gut.39.5.762]

**P- Reviewers**: Frider B, Gow KW, Keese M **S-Editor**: Song XX
**L- Editor**: Roemmele A **E- Editor**: Wu HL

World Journal of Surgical Procedures

Online Submissions: http://www.wjgnet.com/esps/
bpgoffice@wjgnet.com
doi:10.5412/wjsp.v4.i1.21

*World J Surg Proced* 2014 March 28; 4(1): 21-22
ISSN 2219-2832 (online)


CASE REPORT

# Notaras procedure for incarcerated rectal prolapse

Mutlu Unver, Safak Ozturk, Osman Bozbıyık, Varlık Erol, Gökhan Akbulut

Mutlu Unver, Safak Ozturk, Osman Bozbıyık, Varlık Erol, Gökhan Akbulut, Department of General Surgery, Tepecik Education and Research Hospital, 35100 Bornova, Izmir, Turkey
Author contributions: Unver M and Ozturk S contributed to the letter's conception and design, acquisition of data and drafting of the manuscript; Bozbiyik O and Erol V contributed to the letter' s conception and design; Akbulut G contributed to revision of this letter.
Correspondence to: Mutlu Unver, MD, Department of General Surgery, Tepecik Education and Research Hospital, 250 sok. No:3/2 kat 7 daire 25 Manavkuyu, 35100 Bornova, İzmir, Turkey. mutluunver@gmail.com
Telephone: +90-505-829866 Fax: +90-232-43056
Received: September 13, 2013 Revised: November 6, 2013
Accepted: November 20, 2013
Published online: March 28, 2014

## Abstract

Patients with an incarcerated rectal prolapse usually present in the emergency department where manual reduction is first attempted. If reduction is unsuccessful, an emergency laparotomy and internal reduction is required. Edema in the rectal and perineal tissues and impaired blood flow are the main factors for a high percentage of anastomotic leaks. The traditional single stage perineal rectosigmoidectomy is not a safe surgical procedure for treating incarcerated or strangulated rectal prolapses associated with severe edema. Herein we report a case of an incarcerated rectal prolapse treated with the Notaras procedure.



**Key words:** Notaras procedure; Rectal prolapse; Incarcerated; Perineal rectosigmoidectomy

**Core tip:** Patients with an incarcerated rectal prolapse usually present in the emergency department where manual reduction is first attempted. If reduction is unsuccessful, an emergency laparotomy and internal reduction is required. Edema in the rectal and perineal tissues and impaired blood flow are the main factors for a high percentage of anastomotic leaks. So, the traditional single stage perineal rectosigmoidectomy is not a safe surgical procedure for treating an incarcerated or strangulated rectal prolapse associated with severe edema. Herein we report a case of an incarcerated rectal prolapse treated with the Notaras procedure.

Unver M, Ozturk S, Bozbıyık O, Erol V, Akbulut G. Notaras procedure for incarcerated rectal prolapse. *World J Surg Proced* 2014; 4(1): 21-22 Available from: URL: http://www.wjgnet.com/2219-2832/full/v4/i1/21.htm DOI: http://dx.doi.org/10.5412/wjsp.v4.i1.21

## INTRODUCTION

Rectal prolapse is defined as intussusception of the rectum through the anal canal. Although known and described as early as 1500 BC[1], there is still uncertainty concerning its clinical definition, course and pathophysiology, which justifies the numerous therapeutic modalities and operations proposed[2]. Commonly, in many centers a single stage perineal rectosigmoidectomy is performed to treat patients with a reducible rectal prolapse. Patients with an incarcerated rectal prolapse usually present in the emergency department where manual reduction is first attempted. Reduction of a large prolapse may be difficult because of significant edema that collects in the rectal tissues. If reduction is unsuccessful, an emergency laparotomy and internal reduction is required. If patients with an acute incarcerated or strangulated rectal prolapse are treated with perineal rectosigmoidectomy, anastomotic leak risk is 25% during the postoperative period[3,4]. Edema in the rectal and perineal tissues and impaired blood flow are the main factors for a high percentage of anastomotic leaks. The traditional single stage perineal rectosigmoidectomy is not a safe surgical procedure for treating an incarcerated or strangulated rectal prolapse associated with severe edema[4].

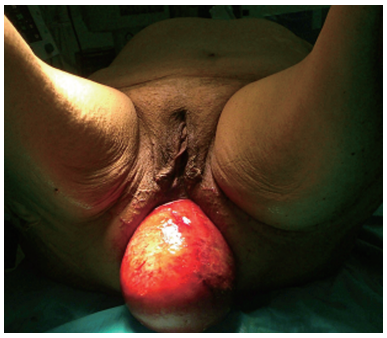

**Figure 1 Edematous and incarcerated rectal prolapse without gangrenous areas.**

## CASE REPORT

In this report, we present a 59-year-old woman with a three year history of Alzheimer's disease. She checked in to the emergency department with a strangulated rectal prolapse which had appeared 3 h prior to consultation. Physical examination revealed a severely edematous and irreducible rectal prolapse without gangrenous areas (Figure 1). Despite sedation, the Trendelenburg position and topical application of sucrose to decrease bowel edema, all attempts for manual reduction were unsuccessful. As a result, we decided to perform a laparotomy. During the laparotomy, we tried internal reduction with external manual reduction again. The last attempt was successful. The prolapsed section was not necrotic, there were no gangrenous areas and blood flow increased. A piece of monofilament synthetic mesh was sutured behind the rectum, covering approximately one-third of its posterior circumference. The upper edge was then sutured to the sacral promontory, as described by Notaras[5]. The patient's postoperative course was uneventful and she was discharged on the 8$^{th}$ postoperative day. At the 6 mo follow-up, there was no recurrence in the rectal prolapse other than a minor constipation problem.

## DISCUSSION

If the incarcerated or strangulated rectal prolapse cannot be manually reduced, a few techniques may help the bowel return to its anatomic position, such as sedation, Trendelenburg position and/or topical applications of salt and sucrose which may decrease bowel edema and enable a natural reduction[6]. The use of an elastic compression wrap can be practiced[7]. Perineal rectosigmoidectomy is a good surgical option in cases complicated by necrosis and poor intestinal blood flow. However, patients with an acute incarcerated or strangulated rectal prolapse have an increased risk of an anastomotic leak compared to other elective operations. After internal and external reduction, waiting a few minutes for a better blood supply if the patient has no complications with necrosis is an excellent option. With a good blood flow, the Notaras procedure, in effect rectopexy, suspends the rectum and the presence of the mesh additionally results in thickening of part of the rectal wall with the result that prolapse of the rectum will be prevented. In conclusion, with a good blood supply and the absence of necrosis, the Notaras procedure can be performed safely in patients with an incarcerated or strangulated rectal prolapse.

## ACKNOWLEDGMENTS

The authors wish to thank Mrs. Crystal A Stang for editing the English of the manuscript.

## COMMENTS

### *Case characteristics*

The patient had pain in the rectum.

### *Clinical diagnosis*

The patient had an irreducible rectal prolapse.

### *Differential diagnosis*

It was a certain diagnosis with no differential diagnosis.

### *Laboratory diagnosis*

Laboratory tests were in the normal range.

### *Treatment*

The patient underwent emergency surgery (Notaras procedure).

### *Related reports*

The second and the fifth references are about the repair of rectal prolapses. These studies may help to understand emergency repair of a rectal prolapse and this case.

### *Term explanation*

Notaras procedure: a piece of monofilament synthetic mesh is sutured behind the rectum, covering approximately one-third of its posterior circumference.

### *Experiences and lessons*

The Notaras procedure can be performed safely in patients with an acute incarcerated or strangulated rectal prolapse in the absence of necrosis.

### *Peer review*

This is an interesting case report suggesting the use of a surgical procedure usually not described in the acute phase.

## REFERENCES

1 **Wu JS**. Rectal prolapse: a historical perspective. *Curr Probl Surg* 2009; **46**: 602-716 [PMID: 19577675]
2 **Voulimeneas I**, Antonopoulos C, Alifierakis E, Ioannides P. Perineal rectosigmoidectomy for gangrenous rectal prolapse. *World J Gastroenterol* 2010; **16**: 2689-2691 [PMID: 20518093]
3 **Ramanujam PS**, Venkatesh KS. Management of acute incarcerated rectal prolapse. *Dis Colon Rectum* 1992; **35**: 1154-1156 [PMID: 1473417]
4 **Fei R**, Chen W, Xiang T, Sheng Q, Wang J, Liu F. A modified two-stage perineal rectosigmoidectomy for incarcerated rectal prolapse. *Tech Coloproctol* 2013; Epub ahead of print [PMID: 23525965 DOI: 10.1007/s10151-013-0996-9]
5 **Notaras MJ**. The use of Mersilene mesh in rectal prolapse repair. *Proc R Soc Med* 1973; **27**: 930
6 **Bastawrous A**, Abcarian H. Complete rectal prolapse. In: Dempsey DT, Klein AS, Pemberton JH, Peters JH, editors. Suckelford's Surgery of the alimentary tract. Volume 2. 6th edition. Philadelphia: Saunders Elsevier, 2007: 1958-1965
7 **Sarpel U**, Jacob BP, Steinhagen RM. Reduction of a large incarcerated rectal prolapse by use of an elastic compression wrap. *Dis Colon Rectum* 2005; **48**: 1320-1322 [PMID: 15789124]

**P- Reviewers:** Chello M, Howard M **S- Editor**: Song XX
**L- Editor**: Roemmele A **E-Editor:** Wu HL

WJSP World Journal of Surgical Procedures

Online Submissions: http://www.wjgnet.com/esps/
bpgoffice@wjgnet.com
www.wjgnet.com

*World J Surg Proced* 2014 March 28; 4(1): I-V
ISSN 2219-2832 (online)


*INSTRUCTIONS TO AUTHORS*

## GENERAL INFORMATION

*World Journal of Surgical Procedures* (*World J Surg Proced*, *WJSP*, online ISSN 2219-2832, DOI: 10.5412) is a peer-reviewed open access (OA) academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

### *Aim and scope*

*WJSP* covers topics concerning ambulatory surgical procedures, cardiovascular surgical procedures, digestive system surgical procedures, endocrine surgical procedures, obstetric surgical procedures, neurosurgical procedures, ophthalmologic surgical procedures, oral surgical procedures, orthopedic procedures, otorhinolaryngologic surgical procedures, reconstructive surgical procedures, thoracic surgical procedures, urogenital surgical procedures, computer-assisted surgical procedures, elective surgical procedures, and minimally invasive, surgical procedures, specifically including ablation techniques, anastomosis, assisted circulation, bariatric surgery, biopsy, body modification, non-therapeutic, curettage, debridement, decompression, deep brain stimulation, device removal, dissection, drainage, electrosurgery, extracorporeal circulation, hemostasis, intraoperative care, laparotomy, ligation, lymph node excision, mastectomy, microsurgery, monitoring, intraoperative, ostomy, paracentesis, pelvic exenteration, perioperative care, postoperative care, preoperative care, prosthesis implantation, reoperation, second-look surgery, splenectomy, suture techniques, symphysiotomy, tissue and organ harvesting, transplantation, diagnostic imaging, and endoscopy. The current columns of *WJSP* include editorial, frontier, diagnostic advances, therapeutics advances, field of vision, mini-reviews, review, topic highlight, medical ethics, original articles, case report, clinical case conference (Clinicopathological conference), and autobiography.

We encourage authors to submit their manuscripts to *WJSP*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

*WJSP* is edited and published by Baishideng Publishing Group (BPG). BPG has a strong professional editorial team composed of science editors, language editors and electronic editors. BPG currently publishes 42 OA clinical medical journals, including 41 in English, has a total of 15 471 editorial borad members or peer reivewers, and is a world first-class publisher.

### *Columns*

The columns in the issues of *WJSP* will include: (1) Editorial: The editorial board members are invited to make comments on an important topic in their field in terms of its current research status and future directions to lead the development of this discipline; (2) Frontier: The editorial board members are invited to select a highly cited cutting-edge original paper of his/her own to summarize major findings, the problems that have been resolved and remain to be resolved, and future research directions to help readers understand his/her important academic point of view and future research directions in the field; (3) Diagnostic Advances: The editorial board members are invited to write high-quality diagnostic advances in their field to improve the diagnostic skills of readers. The topic covers general clinical diagnosis, differential diagnosis, pathological diagnosis, laboratory diagnosis, imaging diagnosis, endoscopic diagnosis, biotechnological diagnosis, functional diagnosis, and physical diagnosis; (4) Therapeutics Advances: The editorial board members are invited to write high-quality therapeutic advances in their field to help improve the therapeutic skills of readers. The topic covers medication therapy, psychotherapy, physical therapy, replacement therapy, interventional therapy, minimally invasive therapy, endoscopic therapy, transplantation therapy, and surgical therapy; (5) Field of Vision: The editorial board members are invited to write commentaries on classic articles, hot topic articles, or latest articles to keep readers at the forefront of research and increase their levels of clinical research. Classic articles refer to papers that are included in Web of Knowledge and have received a large number of citations (ranking in the top 1%) after being published for more than years, reflecting the quality and impact of papers. Hot topic articles refer to papers that are included in Web of Knowledge and have received a large number of citations after being published for no more than 2 years, reflecting cutting-edge trends in scientific research. Latest articles refer to the latest published high-quality papers that are included in PubMed, reflecting the latest research trends. These commentary articles should focus on the status quo of research, the most important research topics, the problems that have now been resolved and remain to be resolved, and future research directions. Basic information about the article to be commented (including authors, article title, journal name, year, volume, and inclusive page numbers; (6) Minireviews: The editorial board members are invited to write short reviews on recent advances and trends in research of molecular biology, genomics, and related cutting-edge technologies to provide readers with the latest knowledge and help improve their diagnostic and therapeutic skills; (7) Review: To make a systematic review to focus on the status quo of research, the most important research topics, the problems that have now been resolved and remain to be resolved, and future research directions; (8) Topic Highlight: The editorial board members are invited to write a series of articles (7-10 articles) to comment and discuss a hot topic to help improve the diagnostic and therapeutic skills of readers; (9) Medical Ethics: The editorial board members are invited to write articles about medical ethics to increase readers' knowledge of medical ethics. The topic covers international ethics guidelines, animal studies, clinical trials, organ transplantation, *etc.*; (10) Clinical Case Conference or Clinicopathological Conference: The editorial board members are invited to contribute high-quality clinical case conference; (11) Original Articles: To report innovative and original findings in surgical procedures; (12) Brief Articles: To briefly report the novel and innovative findings in surgical procedures; (13) Meta-Analysis: Covers the systematic review, mixedtreatment comparison, meta-regression, and overview of reviews, in order to summarize a given quantitative effect, e.g., the clinical effectiveness and safety of clinical treatments by combining data from two or more randomized controlled trials, thereby providing more precise and externally valid estimates than those which would stem from each individual dataset if analyzed separately from the others; (14) Case Report: To report a rare or typical case; (15) Letters to the Editor: To discuss and make reply to the contributions published in *WJSP*, or to introduce and comment on a controversial issue of general interest; (16) Book Reviews: To introduce and comment on quality monographs of surgical procedures; and (17) Autobiography: The editorial board members are invited to write their autobiography to provide readers with stories of success or failure in their scientific research career. The topic covers their basic personal information and information about when they started doing research work, where and how they did research work, what they have achieved, and their lessons from success or failure.

***Name of journal***
*World Journal of Surgical Procedures*

***ISSN***
ISSN 2219-2832 (online)

***Launch date***
December 29, 2011

***Frequency***
Four-monthly



***Editorial office***
Jin-Lei Wang, Director
Xiu-Xia Song, Vice Director
*World Journal of Surgical Procedures*
Room 903, Building D, Ocean International Center,
No. 62 Dongsihuan Zhonglu, Chaoyang District,
Beijing 100025, China
Telephone: +86-10-85381891
Fax: +86-10-85381893
E-mail: bpgoffice@wjgnet.com
http://www.wjgnet.com

***Publisher***
Baishideng Publishing Group Co., Limited
Flat C, 23/F., Lucky Plaza, 315-321 Lockhart Road,
Wan Chai, Hong Kong, China
Telephone: +852-31779906
Fax: +852-65557188
E-mail: bpgoffice@wjgnet.com
http://www.wjgnet.com

***Production center***
Beijing Baishideng BioMed Scientific Co., Limited
Room 903, Building D, Ocean International Center,
No. 62 Dongsihuan Zhonglu, Chaoyang District,
Beijing 100025, China
Telephone: +86-10-85381892
Fax: +86-10-85381893

***Representative office***
USA Office
8226 Regency Drive,
Pleasanton, CA 94588-3144, United States

***Instructions to authors***
Full instructions are available online at http://www.wjgnet.com/2219-2832/g_info_20100722180909.htm.

***Indexed and Abstracted in***
Digital Object Identifier.

## SPECIAL STATEMENT

All articles published in this journal represent the viewpoints of the authors except where indicated otherwise.

***Biostatistical editing***
Statistical review is performed after peer review. We invite an expert in Biomedical Statistics to evaluate the statistical method used in the paper, including *t*-test (group or paired comparisons), chi-squared test, Ridit, probit, logit, regression (linear, curvilinear, or stepwise), correlation, analysis of variance, analysis of covariance, *etc*. The reviewing points include: (1) Statistical methods should be described when they are used to verify the results; (2) Whether the statistical techniques are suitable or correct; (3) Only homogeneous data can be averaged. Standard deviations are preferred to standard errors. Give the number of observations and subjects (*n*). Losses in observations, such as drop-outs from the study should be reported; (4) Values such as ED50, LD50, IC50 should have their 95% confidence limits calculated and compared by weighted probit analysis (Bliss and Finney); and (5) The word 'significantly' should be replaced by its synonyms (if it indicates extent) or the *P* value (if it indicates statistical significance).

***Conflict-of-interest statement***
In the interests of transparency and to help reviewers assess any potential bias, *WJSP* requires authors of all papers to declare any competing commercial, personal, political, intellectual, or religious interests in relation to the submitted work. Referees are also asked to indicate any potential conflict they might have reviewing a particular paper. Before submitting, authors are suggested to read "Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Ethical Considerations in the Conduct and Reporting of Research: Conflicts of Interest" from International Committee of Medical Journal Editors (ICMJE), which is available at: http://www.icmje.org/ethical_4conflicts.html.

Sample wording: [Name of individual] has received fees for serving as a speaker, a consultant and an advisory board member for [names of organizations], and has received research funding from [names of organization]. [Name of individual] is an employee of [name of organization]. [Name of individual] owns stocks and shares in [name of organization]. [Name of individual] owns patent [patent identification and brief description].

***Statement of informed consent***
Manuscripts should contain a statement to the effect that all human studies have been reviewed by the appropriate ethics committee or it should be stated clearly in the text that all persons gave their informed consent prior to their inclusion in the study. Details that might disclose the identity of the subjects under study should be omitted. Authors should also draw attention to the Code of Ethics of the World Medical Association (Declaration of Helsinki, 1964, as revised in 2004).

***Statement of human and animal rights***
When reporting the results from experiments, authors should follow the highest standards and the trial should conform to Good Clinical Practice (for example, US Food and Drug Administration Good Clinical Practice in FDA-Regulated Clinical Trials; UK Medicines Research Council Guidelines for Good Clinical Practice in Clinical Trials) and/or the World Medical Association Declaration of Helsinki. Generally, we suggest authors follow the lead investigator's national standard. If doubt exists whether the research was conducted in accordance with the above standards, the authors must explain the rationale for their approach and demonstrate that the institutional review body explicitly approved the doubtful aspects of the study.

Before submitting, authors should make their study approved by the relevant research ethics committee or institutional review board. If human participants were involved, manuscripts must be accompanied by a statement that the experiments were undertaken with the understanding and appropriate informed consent of each. Any personal item or information will not be published without explicit consents from the involved patients. If experimental animals were used, the materials and methods (experimental procedures) section must clearly indicate that appropriate measures were taken to minimize pain or discomfort, and details of animal care should be provided.

## SUBMISSION OF MANUSCRIPTS

Manuscripts should be typed in 1.5 line spacing and 12 pt. Book Antiqua with ample margins. Number all pages consecutively, and start each of the following sections on a new page: Title Page, Abstract, Introduction, Materials and Methods, Results, Discus-

sion, Acknowledgements, References, Tables, Figures, and Figure Legends. Neither the editors nor the publisher are responsible for the opinions expressed by contributors. Manuscripts formally accepted for publication become the permanent property of Baishideng Publishing Group Co., Limited, and may not be reproduced by any means, in whole or in part, without the written permission of both the authors and the publisher. We reserve the right to copy-edit and put onto our website accepted manuscripts. Authors should follow the relevant guidelines for the care and use of laboratory animals of their institution or national animal welfare committee. For the sake of transparency in regard to the performance and reporting of clinical trials, we endorse the policy of the ICMJE to refuse to publish papers on clinical trial results if the trial was not recorded in a publicly-accessible registry at its outset. The only register now available, to our knowledge, is http://www.clinicaltrials.gov sponsored by the United States National Library of Medicine and we encourage all potential contributors to register with it. However, in the case that other registers become available you will be duly notified. A letter of recommendation from each author's organization should be provided with the contributed article to ensure the privacy and secrecy of research is protected.

Authors should retain one copy of the text, tables, photographs and illustrations because rejected manuscripts will not be returned to the author(s) and the editors will not be responsible for loss or damage to photographs and illustrations sustained during mailing.

### *Online submissions*

Manuscripts should be submitted through the Online Submission System at: http://www.wjgnet.com/esps/. Authors are highly recommended to consult the ONLINE INSTRUCTIONS TO AUTHORS (http://www.wjgnet.com/2219-2832/g_info_20100722180909.htm) before attempting to submit online. For assistance, authors encountering problems with the Online Submission System may send an email describing the problem to bpgoffice@wjgnet.com, or by telephone: +86-10-85381892. If you submit your manuscript online, do not make a postal contribution. Repeated online submission for the same manuscript is strictly prohibited.

## MANUSCRIPT PREPARATION

All contributions should be written in English. All articles must be submitted using word-processing software. All submissions must be typed in 1.5 line spacing and 12 pt. Book Antiqua with ample margins. Style should conform to our house format. Required information for each of the manuscript sections is as follows:

### *Title page*

**Title:** Title should be less than 12 words.

**Running title:** A short running title of less than 6 words should be provided.

**Authorship:** Authorship credit should be in accordance with the standard proposed by ICMJE, based on (1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be published. Authors should meet conditions 1, 2, and 3.

**Institution:** Author names should be given first, then the complete name of institution, city, province and postcode. For example, Xu-Chen Zhang, Li-Xin Mei, Department of Pathology, Chengde Medical College, Chengde 067000, Hebei Province, China. One author may be represented from two institutions, for example, George Sgourakis, Department of General, Visceral, and Transplantation Surgery, Essen 45122, Germany; George Sgourakis, 2nd Surgical Department, Korgialenio-Benakio Red Cross Hospital, Athens 15451, Greece

**Author contributions:** The format of this section should be: Author contributions: Wang CL and Liang L contributed equally to this work; Wang CL, Liang L, Fu JF, Zou CC, Hong F and Wu XM designed the research; Wang CL, Zou CC, Hong F and Wu XM performed the research; Xue JZ and Lu JR contributed new reagents/analytic tools; Wang CL, Liang L and Fu JF analyzed the data; and Wang CL, Liang L and Fu JF wrote the paper.

**Supportive foundations:** The complete name and number of supportive foundations should be provided, *e.g.*, Supported by National Natural Science Foundation of China, No. 30224801

**Correspondence to:** Only one corresponding address should be provided. Author names should be given first, then author title, affiliation, the complete name of institution, city, postcode, province, country, and email. All the letters in the email should be in lower case. A space interval should be inserted between country name and email address. For example, Montgomery Bissell, MD, Professor of Medicine, Chief, Liver Center, Gastroenterology Division, University of California, Box 0538, San Francisco, CA 94143, United States. montgomery.bissell@ucsf.edu

**Telephone and fax:** Telephone and fax should consist of +, country number, district number and telephone or fax number, *e.g.*, Telephone: +86-10-85381892 Fax: +86-10-85381893

**Peer reviewers:** All articles received are subject to peer review. Normally, three experts are invited for each article. Decision on acceptance is made only when at least two experts recommend publication of an article. All peer-reviewers are acknowledged on Express Submission and Peer-review System website.

### *Abstract*

There are unstructured abstracts (no less than 200 words) and structured abstracts. The specific requirements for structured abstracts are as follows:

An informative, structured abstract should accompany each manuscript. Abstracts of original contributions should be structured into the following sections: AIM (no more than 20 words; Only the purpose of the study should be included. Please write the Aim in the form of "To investigate/study/…"), METHODS (no less than 140 words for Original Articles; and no less than 80 words for Brief Articles), RESULTS (no less than 150 words for Original Articles and no less than 120 words for Brief Articles; You should present *P* values where appropriate and must provide relevant data to illustrate how they were obtained, *e.g.*, 6.92 ± 3.86 *vs* 3.61 ± 1.67, $P < 0.001$), and CONCLUSION (no more than 26 words).

### *Key words*

Please list 5-10 key words, selected mainly from *Index Medicus*, which reflect the content of the study.

### *Core tip*

Please write a summary of less than 100 words to outline the most innovative and important arguments and core contents in your paper to attract readers.

### *Text*

For articles of these sections, original articles and brief articles, the main text should be structured into the following sections: INTRODUCTION, MATERIALS AND METHODS, RESULTS and DISCUSSION, and should include appropriate Figures and Tables. Data should be presented in the main text or in Figures and Tables, but not in both.

### *Illustrations*

Figures should be numbered as 1, 2, 3, *etc.*, and mentioned clearly in the main text. Provide a brief title for each figure on a separate page. Detailed legends should not be provided under the figures. This part should be added into the text where the figures are applicable. Keeping all elements compiled is necessary in line-art image. Scale bars should be used rather than magnification factors, with the length of

the bar defined in the legend rather than on the bar itself. File names should identify the figure and panel. Avoid layering type directly over shaded or textured areas. Please use uniform legends for the same subjects. For example: Figure 1 Pathological changes in atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: …*etc*. It is our principle to publish high resolution-figures for the E-versions.

### *Tables*

Three-line tables should be numbered 1, 2, 3, *etc*., and mentioned clearly in the main text. Provide a brief title for each table. Detailed legends should not be included under tables, but rather added into the text where applicable. The information should complement, but not duplicate the text. Use one horizontal line under the title, a second under column heads, and a third below the Table, above any footnotes. Vertical and italic lines should be omitted.

### *Notes in tables and illustrations*

Data that are not statistically significant should not be noted. $^{a}P < 0.05$, $^{b}P < 0.01$ should be noted ($P > 0.05$ should not be noted). If there are other series of $P$ values, $^{c}P < 0.05$ and $^{d}P < 0.01$ are used. A third series of $P$ values can be expressed as $^{e}P < 0.05$ and $^{f}P < 0.01$. Other notes in tables or under illustrations should be expressed as $^{1}$F, $^{2}$F, $^{3}$F; or sometimes as other symbols with a superscript (Arabic numerals) in the upper left corner. In a multi-curve illustration, each curve should be labeled with ●, ○, ■, □, ▲, △, *etc*., in a certain sequence.

### *Acknowledgments*

Brief acknowledgments of persons who have made genuine contributions to the manuscript and who endorse the data and conclusions should be included. Authors are responsible for obtaining written permission to use any copyrighted text and/or illustrations.

## REFERENCES

### *Coding system*

The author should number the references in Arabic numerals according to the citation order in the text. Put reference numbers in square brackets in superscript at the end of citation content or after the cited author's name. For citation content which is part of the narration, the coding number and square brackets should be typeset normally. For example, "Crohn's disease (CD) is associated with increased intestinal permeability[1,2]". If references are cited directly in the text, they should be put together within the text, for example, "From references[19,22-24], we know that..."

When the authors write the references, please ensure that the order in text is the same as in the references section, and also ensure the spelling accuracy of the first author's name. Do not list the same citation twice.

### *PMID and DOI*

Pleased provide PubMed citation numbers to the reference list, *e.g*., PMID and DOI, which can be found at http://www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed and http://www.crossref.org/SimpleTextQuery/, respectively. The numbers will be used in E-version of this journal.

### *Style for journal references*

Authors: the name of the first author should be typed in bold-faced letters. The family name of all authors should be typed with the initial letter capitalized, followed by their abbreviated first and middle initials. (For example, Lian-Sheng Ma is abbreviated as Ma LS, Bo-Rong Pan as Pan BR). The title of the cited article and italicized journal title (journal title should be in its abbreviated form as shown in PubMed), publication date, volume number (in black), start page, and end page [PMID: 11819634 DOI: 10.3748/wjg.13.5396].

### *Style for book references*

Authors: the name of the first author should be typed in bold-faced letters. The surname of all authors should be typed with the initial letter capitalized, followed by their abbreviated middle and first initials. (For example, Lian-Sheng Ma is abbreviated as Ma LS, Bo-Rong Pan as Pan BR) Book title. Publication number. Publication place: Publication press, Year: start page and end page.

### *Format*

**Journals**

*English journal article (list all authors and include the PMID where applicable)*

1 **Jung EM**, Clevert DA, Schreyer AG, Schmitt S, Rennert J, Kubale R, Feuerbach S, Jung F. Evaluation of quantitative contrast harmonic imaging to assess malignancy of liver tumors: A prospective controlled two-center study. *World J Gastroenterol* 2007; **13**: 6356-6364 [PMID: 18081224 DOI: 10.3748/wjg.13.6356]

*Chinese journal article (list all authors and include the PMID where applicable)*

2 **Lin GZ**, Wang XZ, Wang P, Lin J, Yang FD. Immunologic effect of Jianpi Yishen decoction in treatment of Pixu-diarrhoea. *Shijie Huaren Xiaohua Zazhi* 1999; **7**: 285-287

*In press*

3 **Tian D**, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. *Proc Natl Acad Sci USA* 2006; In press

*Organization as author*

4 **Diabetes Prevention Program Research Group**. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002; **40**: 679-686 [PMID: 12411462 PMCID:2516377 DOI:10.1161/01.HYP.0000035706.28494.09]

*Both personal authors and an organization as author*

5 **Vallancien G**, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1, 274 European men suffering from lower urinary tract symptoms. *J Urol* 2003; **169**: 2257-2261 [PMID: 12771764 DOI:10.1097/01.ju.0000067940.76090.73]

*No author given*

6 21st century heart solution may have a sting in the tail. *BMJ* 2002; **325**: 184 [PMID: 12142303 DOI:10.1136/bmj.325.7357.184]

*Volume with supplement*

7 **Geraud G**, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. *Headache* 2002; **42** Suppl 2: S93-99 [PMID: 12028325 DOI:10.1046/j.1526-4610.42.s2.7.x]

*Issue with no volume*

8 **Banit DM**, Kaufer H, Hartford JM. Intraoperative frozen section analysis in revision total joint arthroplasty. *Clin Orthop Relat Res* 2002; (**401**): 230-238 [PMID: 12151900 DOI:10.1097/00003086-200208000-00026]

*No volume or issue*

9 Outreach: Bringing HIV-positive individuals into care. *HRSA Careaction* 2002; 1-6 [PMID: 12154804]

**Books**

*Personal author(s)*

10 **Sherlock S**, Dooley J. Diseases of the liver and billiary system. 9th ed. Oxford: Blackwell Sci Pub, 1993: 258-296

*Chapter in a book (list all authors)*

11 **Lam SK**. Academic investigator's perspectives of medical treatment for peptic ulcer. In: Swabb EA, Azabo S. Ulcer disease: investigation and basis for therapy. New York: Marcel Dekker, 1991: 431-450

*Author(s) and editor(s)*

12 **Breedlove GK**, Schorfheide AM. Adolescent pregnancy. 2nd ed. Wieczorek RR, editor. White Plains (NY): March of Dimes Education Services, 2001: 20-34

*Conference proceedings*

13 **Harnden P**, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ cell tumours Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer, 2002: 30-56

*Conference paper*

14 **Christensen S**, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA,

Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer, 2002: 182-191

**Electronic journal** (list all authors)

15 Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: http://www.cdc.gov/ncidod/eid/index.htm

**Patent** (list all authors)

16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

### *Statistical data*

Write as mean ± SD or mean ± SE.

### *Statistical expression*

Express *t* test as *t* (in italics), *F* test as *F* (in italics), chi square test as $\chi^2$ (in Greek), related coefficient as *r* (in italics), degree of freedom as υ (in Greek), sample number as *n* (in italics), and probability as *P* (in italics).

### *Units*

Use SI units. For example: body mass, m (B) = 78 kg; blood pressure, p (B) = 16.2/12.3 kPa; incubation time, t (incubation) = 96 h, blood glucose concentration, c (glucose) 6.4 ± 2.1 mmol/L; blood CEA mass concentration, p (CEA) = 8.6 24.5 μg/L; $CO_2$ volume fraction, 50 mL/L $CO_2$, not 5% $CO_2$; likewise for 40 g/L formaldehyde, not 10% formalin; and mass fraction, 8 ng/g, *etc.* Arabic numerals such as 23, 243, 641 should be read 23 243 641.

The format for how to accurately write common units and quantums can be found at: http://www.wjgnet.com/2219-2832/g_info_20100725073806.htm.

### *Abbreviations*

Standard abbreviations should be defined in the abstract and on first mention in the text. In general, terms should not be abbreviated unless they are used repeatedly and the abbreviation is helpful to the reader. Permissible abbreviations are listed in Units, Symbols and Abbreviations: A Guide for Biological and Medical Editors and Authors (Ed. Baron DN, 1988) published by The Royal Society of Medicine, London. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, mAb, can be used directly without further explanation.

### *Italics*

Quantities: *t* time or temperature, *c* concentration, *A* area, *l* length, *m* mass, *V* volume.
Genotypes: *gyrA*, *arg* 1, *c myc*, *c fos*, *etc.*
Restriction enzymes: *Eco*RI, *Hin*dI, *Bam*HI, *Kbo* I, *Kpn* I, *etc.*
Biology: *H. pylori*, *E coli*, *etc.*

### *Examples for paper writing*

All types of articles' writing style and requirement will be found in the link: http://www.wjgnet.com/esps/NavigationInfo.aspx?id=15

## RESUBMISSION OF THE REVISED MANUSCRIPTS

Authors must revise their manuscript carefully according to the revision policies of Baishideng Publishing Group Co., Limited. The revised version, along with the signed copyright transfer agreement, responses to the reviewers, and English language Grade A certificate (for non-native speakers of English), should be submitted to the online system *via* the link contained in the e-mail sent by the editor. If you have any questions about the revision, please send e-mail to esps@wjgnet.com.

### *Language evaluation*

The language of a manuscript will be graded before it is sent for revision. (1) Grade A: priority publishing; (2) Grade B: minor language polishing; (3) Grade C: a great deal of language polishing needed; and (4) Grade D: rejected. Revised articles should reach Grade A.

### *Copyright assignment form*

Please download a Copyright assignment form from http://www.wjgnet.com/2219-2832/g_info_20100725073726.htm.

### *Responses to reviewers*

Please revise your article according to the comments/suggestions provided by the reviewers. The format for responses to the reviewers' comments can be found at: http://www.wjgnet.com/2219-2832/g_info_20100725073445.htm.

### *Proof of financial support*

For papers supported by a foundation, authors should provide a copy of the approval document and serial number of the foundation.

## STATEMENT ABOUT ANONYMOUS PUBLICATION OF THE PEER REVIEWERS' COMMENTS

In order to increase the quality of peer review, push authors to carefully revise their manuscripts based on the peer reviewers' comments, and promote academic interactions among peer reviewers, authors and readers, we decide to anonymously publish the reviewers' comments and author's responses at the same time the manuscript is published online.

## PUBLICATION FEE

*WJSP* is an international, peer-reviewed, OA online journal. Articles published by this journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium and format, provided the original work is properly cited. The use is non-commercial and is otherwise in compliance with the license. Authors of accepted articles must pay a publication fee. Publication fee: 600 USD per article. All invited articles are published free of charge.

百世登

Baishideng®

Published by **Baishideng Publishing Group Co., Limited**
Flat C, 23/F., Lucky Plaza, 315-321 Lockhart Road,
Wan Chai, Hong Kong, China
Fax: +852-65557188
Telephone: +852-31779906
E-mail: bpgoffice@wjgnet.com
http://www.wjgnet.com