

# The Infectious Complications of Interventional Radiology Based Procedures in Gastroenterology and Hepatology

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## Abstract

**Background and aims.** Many interventional radiology (IR) procedures are used to manage gastroenterological and hepatobiliary diseases. One of the most common complications of any IR procedure is infection. **Methods.** Literature published in English from January 1960 to August 2010 pertaining to the infectious complications of IR in gastroenterology and hepatology patients was examined by electronic search (Medline and the National Library of Medicine, Embase and the Cochrane Library). **Results.** Percutaneous transhepatic cholangiogram (PTC) and biliary drainage, trans-arterial chemoembolization (TACE), transjugular intrahepatic portosystemic shunting (TIPS), imaged guided drainage of an intra-abdominal abscess and radiologically inserted gastrostomy (RIG) are the most common IR procedures performed for gastroenterology and hepatology patients. Procedures such as PTC have a high rate of infection. Infectious complications of TACE and TIPS are uncommon but when they occur, they can be devastating. RIG procedures are also rarely complicated by infection and such infections are generally mild. Use of prophylactic antibiotics is recommended for most of the above procedures. **Conclusion.** The increased availability of IR based gastrointestinal and hepatobiliary techniques means that their related infectious complications will inevitably become more common. It is vital that clinicians be aware of the aetiology, timing and treatment of any potential infections in the peri-procedure period.

## Keywords

Interventional radiology – infectious complications – antibiotic prophylaxis – gastroenterology – hepatology.

## Introduction

Since its inception in the mid 1970s, interventional radiology (IR) has developed into a medical sub-speciality with an ever expanding number of techniques at its disposal. Many IR procedures are used to manage gastroenterological and hepatobiliary diseases. As the frequency with which patients are treated by the interventional radiologist increases, so it is necessary for the clinician to be familiar with the post procedure care and possible complications in such patients. One of the most common complications of any IR procedure is infection. This paper aims to briefly describe the technical aspects of the most commonly performed IR procedures which pertain to gastroenterology and hepatology, and to provide a detailed overview of the potential peri-procedural infectious complications.

## Methods

Literature published in English from January 1960 to August 2010 pertaining to the infectious complications of interventional radiology was examined by an electronic search (Medline and the National Library of Medicine, Embase and the Cochrane Library) using the keywords 'interventional radiology', 'infectious complications', 'antibiotic prophylaxis', 'percutaneous transhepatic cholangiogram', 'trans-arterial chemoembolization', 'transjugular intrahepatic portosystemic shunting' and 'radiologically inserted gastrostomy'. The search was performed independently by two reviewers (D.H. and W.C.T.) between July 2010 and August 2010. Potentially relevant papers were selected based on title and abstract. Additional articles were identified by cross-referencing from papers retrieved in the initial search and the author's personal collections.

## Results / Discussion

### Percutaneous transhepatic cholangiogram and biliary drainage

Percutaneous transhepatic cholangiogram (PTC)

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and biliary drainage are most frequently indicated in the treatment of malignant biliary obstruction, although benign obstruction may also be managed in this manner. In addition to relieving obstruction, it offers diagnostic benefits, providing radiological delineation of an obstructed system and in some cases cytological evidence of underlying malignancy.

#### **Technical aspects**

With the patient in the supine position a 21G needle is inserted in the mid axillary line. It is then passed cranially towards the xiphisternum through the liver parenchyma under fluoroscopic guidance. In increments the needle is advanced, with iodinated contrast being instilled at intervals to confirm needle position within the biliary system. When the biliary tree has been entered, wire access is obtained via the 21G needle. Once the wire is in place, a wire exchange is performed to allow insertion of a drainage catheter, usually 6 French in size. Once inserted, the drainage catheter can be used as the starting point to dilate biliary strictures, insert biliary stents, and remove stones, usually at a later date [1].

#### **Infectious complications**

Infectious complications during PTC are probably the most common of any interventional procedure. When classifying the sterility of interventional procedures, bile duct drainages will be categorized as “dirty” in up to 30% of cases of malignant obstructions and 60% of benign obstructions. In the latter instance, the risk of infectious complication can be as high as 40%. At best, biliary drainage can be classified as a “clean/contaminated procedure” [2]. In addition many patients attending for this procedure have advanced malignancy and may have established sepsis prior to operating. The complication rate, including infection is lower in patients with benign disease [2]. The mortality rate for biliary drainage is approximately 2%, sepsis and hemorrhage being the two leading causes of death [2]. The proliferation of IR means that the importance of percutaneous biliary drainage as a cause of biliary infection has substantially increased. Some centers have reported that radiological intervention has replaced choledocholithiasis as the most common cause of severe cholangitis [3].

The precipitation of sepsis is felt to be due to mechanical agitation of an infected biliary system causing bacteremia. In addition, the passage of a needle through the liver has the potential to provide temporary communication between the biliary system and the surrounding vasculature, allowing a passage of bacteria from the infected bile into the blood. The use of ultrasound guidance rather than fluoroscopic guidance to obtain biliary access, can reduce the number of passes required through the liver [4]. This could in turn result in less agitation of bile and fewer infective complications. Risk factors for developing sepsis include bilioenteric anastomosis and previous instrumentation [5]. Risk factors for contamination of the bile prior to intervention include older age, diabetes, acute cholecystitis and previous biliary surgery [6]. Clearly many patients presenting for PTC will fall into at least one of these demographic groups.

In cases of fatal biliary sepsis of any kind, the most common causative organisms are *E.Coli* and *clostridium*, which account for 75% of cases [5], although one group found that enterococcus is the most likely organism to be cultured from the blood post biliary intervention [6]. Other organisms commonly isolated from the biliary tree include *klebsiella*, *enterobacter cloacae*, *streptococcus viridans*, *bacteroides* and various yeasts [7].

Because of the high rate of infectious complications the routine use of prophylactic antibiotics is advocated. Even in patients with theoretically adequate antibiotic coverage, organisms can often be cultured from blood samples post biliary drainage [6]. This may be due to inadequate choice or timing of antibiotics or because of a large bacterial load following manipulation. There is little agreement in the literature regarding the most appropriate coverage for biliary procedures; however, the high rate of biliary excretion of third generation cephalosporins means they are ideal for use as an antibiotic prophylaxis in biliary procedures. Alternatively ampicillin/sulbactam can be given, this having a greater activity against *enterococcus spp* [7]. In the absence of sepsis, antibiotic cover should continue until the system is fully drained.

#### **Trans-arterial chemoembolization**

The embolization of an organ or part of an organ is a well established technique for treating a variety of benign and malignant disease. The development of chemoembolization as a treatment for hepatic metastases has represented a significant advance in the management of a variety of oncological diseases. Hepatic necrosis and abscess formation are infrequent complications of this procedure. However, when they do occur the sequelae can be devastating. The reported rate of abscess formation post trans-arterial chemoembolization (TACE) is 2.6% or less; however, the mortality rate when this occurs can be up to 50% [8-11].

#### **Technical aspects**

When performing TACE, arterial access is obtained using a femoral approach. An aortogram is initially performed. The coeliac axis is entered using a guide wire and a selective catheter. The hepatic artery is assessed in a similar fashion and ultimately a sub-selective catheter is used to access the vessel feeding the tumour. Once the catheter is in the correct position, embolization material mixed with iodinated contrast is instilled under fluoroscopic guidance. A variety of embolization materials are used. The general approach is to instil drug eluting beads loaded with a chemotherapeutic agent specific to the tumour being treated.

#### **Infective complications**

The necrotic hepatic tissue which forms post-embolization may act as an infective nidus. The primary mechanism for infection in hepatic embolization procedures is most likely contamination of the embolized segment of hepatic parenchyma with biliary pathogens. Cultured organisms are frequently enteric in origin and previous biliary disruption is strongly associated with a risk of abscess formation [8, 12]. Reduced blood flow in larger hepatic vessels during embolization, causes diversion of chemoembolic agents

into the biliary vasculature. This results in local toxicity, and ultimately bile duct damage. The reduced flow which can result in the above effect is commonly seen in metastatic neuroendocrine tumors (caused by spasm or occlusion of the artery and likely mediated by hormonal factors). In one series evaluating embolic treatment of hepatic tumours all patients with abscess formation had neuroendocrine liver metastases [8]. A similarly increased rate of infection has been demonstrated in patients with sarcoma metastases, although the mechanism in these cases is not clear [12]. Previous radiological or surgical biliary intervention is the biggest risk factor for abscess formation. This is likely due to a combination of the underlying disruption to the biliary vasculature being further aggravated by embolization [8], and reflux of organisms in patients with biliary stents. The relative risk for developing a liver abscess in patients who have undergone stent placement, sphincterotomy or bile duct altering surgery compared to those without previous biliary intervention is 894 [13, 14].

Fever, chills and right upper quadrant pain are the most likely presenting symptoms. It should be remembered that these symptoms are commonly present in patients with post embolization syndrome (PES). However, persistence of symptoms for longer than 1 week should raise suspicion of infective complication rather than PES. There is wide variety in the reported time scale for development of abscess post procedure. In the literature, time to development of abscess varies from the first few days post TACE, up to 8 weeks [8, 9]. Therefore a high index of suspicion should be maintained in patients presenting with pyrexia for up to 3 months post TACE [13].

The relative rarity of infection is likely due to the judicious use of prophylactic antibiotic therapy in these patients. Antibiotics should be commenced prior to the procedure. Many authors advocate a 7 day course of treatment. Standard antibiotic prophylaxis varies from centre to centre, both in terms of length of treatment and antimicrobial used. A sample regimen would include cefazolin/metronidazole pre procedure, followed by the same combination until discharge, with amoxicillin/clavulanate for 5 days post discharge [7].

Some investigators have assessed the use of more aggressive antimicrobial prophylaxis in the subset of patients with an abnormal biliary system. Patel et al started treatment, in a small cohort of patients, with levofloxacin 500mg once daily and metronidazole 500mg twice daily 2 days before embolization, continued until 2 weeks after discharge. A bowel preparation of neomycin and erythromycin was also given. There was a trend towards a reduced rate of abscess formation in patients receiving this regimen [13]. Geshwind et al compared a more aggressive regime of tazobactam/piperacillin intravenously 36 hours prior to embolization plus bowel preparation with neomycin and erythromycin with a standard regime of cephalexin. Again this was a small study, but a reduced rate of infection was demonstrated in the experimental group [15]. These results seem to indicate that a more intensive antibiotic regimen should be considered in high risk patients.

### Transjugular intrahepatic portosystemic shunting

Transjugular intrahepatic portosystemic shunting (TIPS) has become an established treatment for cirrhotic patients with uncontrollable variceal haemorrhage. This percutaneous procedure creates an intrahepatic shunt between a branch of the portal vein and the systemic circulation. Patients undergoing TIPS are generally acutely unwell and frequently suffering from multi-organ failure. Infection is poorly tolerated in this immunocompromised patient group.

#### Technical aspects

The right internal jugular vein is accessed under ultrasound guidance, using a 21 gauge needle, a microwire and a 4 French venous sheath. The right hepatic vein is preferentially accessed. A TIPS needle, consisting of a curved inner needle and an outer catheter, is then inserted into the hepatic vein. To identify the portal vein, fluoroscopy alone is generally used, although other methods including ultrasound can be employed. The needle tip is turned anteromedially and advanced caudally out of the hepatic vein for approximately 5cm. When the portal system is entered a guidewire is passed into the mesenteric vein. The tract is dilated using a balloon. Once dilated a bridging stent is deployed. If the portal varices remain full, they may be selectively embolized. If the portal pressures remain high, a second parallel stent may be inserted using a separate hepatic vein [16].

#### Infective complications

Post TIPS bacteraemia has been documented in up to 35% of patients [17] and pyrexia is seen in approximately 10% of patients in the peri-procedural period. This may be caused by mesenteric bacteria seeding the systemic circulation, although an inflammatory reaction in the liver due to stent placement has also been postulated as a possible aetiology for patient pyrexia [18]. Sustained bacteraemia is not as common, the incidence being approximately 7/1000 procedures performed. Sustained bacteraemia may result from thrombus formation within the stent allowing bacteria to seed the neointima [17, 19, 20]. Patients receiving multiple stents and those with central venous catheters in situ appear to be at higher risk of developing infection. Consideration should be given to removal of central venous catheters which are not absolutely necessary in the aftermath of a TIPS procedure [21].

Several organisms are known to cause post TIPS bacteraemia and infection. These include *enterococcus faecalis*, *staphylococcus aureus*, *lactobacillus acidophilus*, *gamella morbillorum*, *escherichia coli*, *klebsiella*, *acinetobacter*, *S. Sanguis*, *S. Bovis* and *candida albicans*. The majority of cases are caused by enteric organisms [17, 19, 20]. The average time lag between stent placement and clinically manifested infection is approximately 9 months. At presentation most patients have conjugated hyperbilirubinaemia, tender hepatomegaly and fever [19].

It has been suggested that this type of infection should be treated in a similar manner to prosthetic valve endocarditis, with sustained antibiotic therapy tailored to a cultured organism [17]. Studies evaluating antibiotic prophylaxis for

TIPS procedures have yielded conflicting results. Despite this their use is widespread. A once off dose of ceftriaxone 1g or 2g has been shown to reduce rate of post TIPS infection [22]. Cefotim, meanwhile, has demonstrated itself ineffective in this regard [21]. The most common agents used are third generation cephalosporins, although it has been noted that they provide inadequate cover against *enterococcus faecalis*, one of the most commonly implicated organisms [7]. Some groups have used the addition of vancomycin as better gram positive cover against skin flora.

### **Radiologically guided drainage of intra-abdominal abscesses**

Intra-abdominal abscess formation is a recognised complication of several gastroenterological diseases. Radiologically guided drainage procedures have, in the majority of such cases, removed the need for a more invasive surgical approach to abscess drainage. While computed tomography is often used, ultrasound (US) is probably the modality most frequently utilized as a guiding tool.

The potential for US probes to transmit infection is well recognised [23, 24]. Up to two thirds of swabs taken from an ultrasound probe may ultimately culture bacteria [25]. The use of US therefore poses an infective risk in the intervention room. No consensus exists regarding the most appropriate way to prevent patient to patient contamination via the US probe, although it is acknowledged that manufacturer's guidelines requiring the immersion of a probe in cleaning solution for 20 minutes post imaging are impractical in a functioning radiology department. Some groups have suggested wiping the surface of the probe with a single clean paper towel until visibly clean. However, improved results are obtained when two paper towels are used consecutively and then followed by cleaning with an alcohol wipe. It is recommended that this double cleaning technique be used in high risk patients [23].

Aside from the above precautions, additional measures are taken to ensure sterility in interventional procedures. Ultrasound requires the presence of coupling gel to transmit the US waves from the probe to the patients' tissue. In routine practice the gel used is non sterile. In the intervention room, however, sterile gel is used in the form of single use sachets. Additionally a sterile plastic cover is used to cover the US probe and the control panel of the US machine. It is common practice to routinely scan the area to be drained prior to adopting full sterile precautions. This is both to ensure that the radiological characteristics of the abscess render it amenable to drainage and to plan an entry route. While ultrasound gel is known to allow the growth of bacteria [24], it has been shown that its use pre biopsy does not result in increased rates of biopsy site sepsis. In terms of the location of the drainage, there is increased post biopsy bacterial growth from covered sites such as the abdomen when compared to exposed areas such as the neck. Similarly increased levels of bacterial growth can be demonstrated in areas with increased numbers of hair and skin folds such as the axilla. Therefore particular care to aseptic technique is required in these locations [26].

### **Radiologically inserted gastrostomy**

The technique of percutaneous radiologically inserted gastrostomy (RIG) was pioneered in the early 1980's. It offers an alternative to endoscopically inserted gastrostomy. The infectious complications of RIG insertion are rare.

#### **Technical aspects**

The patient is prepared by administering oral contrast to outline the transverse colon and by using US to outline the left lobe of the liver. The stomach is distended using a nasogastric tube. It is then punctured using an 18G needle. The stomach wall is pulled against the anterior abdominal wall using a 't-fastener' device. A guidewire is then inserted and the access tract is dilated to the appropriate size. The RIG is then inserted over the guidewire, and stitched in place. The size of the RIG tube can vary from 9 French to 24 French.

#### **Infectious complications**

The rate of infectious complications of RIG insertion varies from 0.3% - 2.3% [27-29]. In patients with ascites, the rate is 7.7 times higher than in those without [28]. Infections are usually minor and localised to the surrounding skin. They can often be treated with topical antimicrobial agents but may require systemic treatment if severe. RIG insertion has the advantage over percutaneous endoscopic gastrostomy (PEG) tubes that it does not require passage of the feeding tube through the mouth and oesophagus and therefore is less likely to become contaminated with upper gastrointestinal tract organisms. The rate of local infection is up to 9 times higher in PEG insertion when compared to RIG30. A further type of radiologically inserted feeding tube, per-oral image-guided gastrostomy (PIG) has a similar rate of infection to RIG. Prophylactic antibiotic use significantly reduces the infection rate in orally placed gastrostomies but their benefit in RIG insertion is not as clear. There are some data to suggest that the use of third generation cephalosporins reduces the rate of post procedure infection in certain patient population [29].

### **Conclusion**

The increased availability of IR based gastrointestinal and hepatobiliary techniques means that their related infectious complications will inevitably become more common. Although these procedures are performed in the interventional suite, it is vital that referring clinicians be aware of the aetiology, timing and treatment of any potential infections in the peri-procedure period.

### **Conflicts of interest**

None to declare.

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