**Helicobacter pylori** and upper gastrointestinal bleed in heart valve surgery

W.L. Liew*, R.K. Walesby

Department of Cardiothoracic Surgery, The London Chest Hospital, Bonner Road, London E2 9JX, UK

Received 30 September 1997; revised version received 3 March 1998; accepted 18 March 1998

**Abstract**

**Objective:** This study was designed to evaluate objectively the incidence of *Helicobacter pylori* infection and upper gastrointestinal (GI) bleeding in patients following heart valve replacement surgery. Since the discovery of *Helicobacter pylori*, its association with gastritis, peptic ulceration and upper GI bleed have been extensively studied. Anticoagulation of patients with mechanical heart valve prostheses is a prerequisite for the prevention of valve thrombosis and thrombo-embolic events. However anticoagulation can have its complications, notably that of upper GI bleeding.

**Methods:** Patients were assessed in routine postoperative outpatient clinics following cardiac valve replacement surgery. This assessment comprised initially of a questionnaire reflecting the symptomatology of upper GI bleeding and its subsequent management. With informed consent, a small sample of blood was obtained by stilette. The *Helicobacter pylori* status was assessed by measuring the presence of antibodies (immunoglobins) to *Helicobacter pylori* in a commercially available test kit, the Rapid Helisal Test. In this preliminary study 150 consecutive patients were scrutinised and their responses to the questionnaire were collected and compared with the Helisal test.

**Results:** From the 150 patients studied, 37 patients were found to be positive to the Helisal test for *Helicobacter pylori* infection, representing 24.6% of all the cohorts. Of these 37 patients, eight gave a positive history of upper GI bleed; five requiring hospital admission with three requiring urgent upper GI endoscopy. Although these eight patients represent only 4.4% of the total group, it is significant to note that this represents 21.6% of those patients found to be *Helicobacter pylori* positive. There were no GI complications in any of those tested negative. There was an increasing incidence of *Helicobacter pylori* infection in the older age group of patients.

**Conclusions:** *Helicobacter pylori* infection is a common infection with serious consequences in heart valve surgery. For those requiring anticoagulation, the incidence of serious consequential upper GI bleed is significantly higher in the presence of this infection. Preoperative or immediate postoperative eradication of the organism is mandatory in those patients requiring indefinite anticoagulation.

© 1998 Published by Elsevier Science B.V. All rights reserved

**Keywords:** Helicobacter pylori; Upper gastrointestinal bleed; Anticoagulation

1. Introduction

Since the discovery of *Helicobacter pylori* (HP) by a multidisciplinary team in Western Australia in 1983 by Marshall and Warren [1–3], the organism has become the most common world-wide human infective agent, affecting over 50% of the world’s population [4–8]. It is a Gram negative fastidious, microaerophilic spiral bacterium and is currently thought to be responsible for almost all cases of chronic non-immune gastritis. Consequently it is thought to have an association with some gastric and oesophageal cancer [9–12] and is today classified as a Class I carcinogen by the WHO [18].

The most reliable way of diagnosing *Helicobacter pylori* infection is by a combination of culture, histology and urease testing of endoscopic biopsies of the gastric antrum [16]. Recently, several diagnostic tests have been introduced which do not require endoscopy and are therefore simpler, cheaper and more acceptable to patients. Two main types are available: breath tests, which rely on *Helicobacter pylori*’s urease activity and serological tests, which measure the host’s immune response to infection [16]. Radioactive carbon-14 breath test has remain the gold standard in the assessment of active *Helicobacter pylori* infection in that the labelled ammonia is liberated from the labelled urea only in the presence of active infec-
tion. This test was not adopted in this study as it involves fasting patients for 8–12 h prior to the test, a longer test duration with results only available at an interval of weeks and more importantly, this test is currently not licensed in the UK.

Anticoagulation is mandatory for patients with mechanical heart valve prostheses for the prevention of valve thrombosis and life-threatening thrombo-emboli events. This therapy has a price which with some authors reporting an incidence of 10–35% of patients developing significant upper GI bleed following anticoagulation [13–15]. In this study, the incidence of Helicobacter pylori and upper GI bleed in patients following heart valve replacement surgery were evaluated to test the hypothesis that Helicobacter pylori infection in the presence of adequate anticoagulation can further predispose susceptible patients to upper GI bleed.

2. Materials and methods

One hundred and fifty patients following heart valve surgery were recruited for this study. They all had undergone left heart valve replacement surgery within the previous 5 years (1991–1996).

All the patients were assessed in the outpatient clinics whereby a set of questions from a standard questionnaire pertinent to upper-gastric symptoms was utilized and the answers recorded. Of particular note, a history of upper GI symptoms, INR and the dose of Warfarin taken were noted. The GI symptoms asked include dyspepsia, nausea, vomiting, waterbrash and frank haematemesis. The type of prosthesis implanted and the position of implantation were also noted.

Following an informed consent, a small sample of blood was taken for commercially available enzyme-linked immunosorbent assay test for the detection of Helicobacter pylori infection.

Helicobacter pylori inhabits exclusively in the mucus layer overlying the gastric epithelium. A unique feature of this organism is its possession of a powerful urea-splitting enzyme and generation of the ammonium radical NH₃. This accounts for its ability to survive in the acidic environment of the stomach by raising the pH of its immediate microenvironment, thereby protecting itself from any acidic denaturation. It also serves to enable itself to reach the protective zone underneath the gastric mucosa where it resides at a pH approaching neutral.

In addition this organism is highly antigenic and does stimulate a severe inflammatory response. This forms the rationale behind the development of the enzyme-linked immunosorbent assay (ELISA), a technique for detecting serum immunoglobins to Helicobacter pylori reliably with good specificity and sensitivity. The rapid Helisal test is one of such tests available commercially with 80–99% sensitivity and 86–99% specificity [17]. This serological kit uses finger capillary blood and does not require the separation of serum. A clear advantage of this method is that it does not require laboratory support, thereby, allowing the result to be obtained within minutes.

The test with the ultimate specificity and sensitivity would be that of PCR (Polymerase Chain Reaction) which shall supersede all the current available tests. This method has the capability of amplifier tiny amounts of specific ‘target’ DNA (H. pylori) so that they can be detected on gels or by DNA hybridization. This DNA polymerase will produce the complementary DNA strand if an exact piece of single-stranded Helicobacter pylori DNA is present.

3. Results

In this preliminary study on 150 consecutive patients (male = 70, female = 80), a total of 37 patients were found to be positive to the Helisal test. The age range of the patients was 50–86 (mean 73.4 years old). This represents 24.6% of the total patients. Out of these 37 patients, eight were found to have symptomatic upper GI bleed; five requiring hospital admission with blood transfusion and three requiring emergency on-table endoscopy.

Dividing the patients into distinct groups with either mechanical or bioprosthetic valves, there were 107 patients in the mechanical group and 43 in the bioprosthetic group.

In the mechanical group of 107 valves, 77 of the valves were placed in the aortic position and 22 in the mitral position. There were none with double valve replacements. There was equivalence of the sexes (56 males, 51 females). From this group, 30 patients were found positive to the Helisal test representing 28.0% of the mechanical replacements. All the seven patients who had upper GI bleed were identified as belonging to the group of patients testing positive to the Helisal test. Although this figure represents only 6.5% of all the patients in the mechanical valve group, it represents seven of 30 patients or 23.3% of all those who were Helisal positive.

Adopting Fisher’s exact test to upper gastrointestinal bleed and Helicobacter pylori infection to a two by two contingency table (8/29 0/113), produces a statistically significant result $P = 0.001$. Females were found to have a greater predilection to Helicobacter pylori infection, but males who had the infection are twice as likely to develop upper GI symptoms.

In the bioprosthetic group, there were 43 patients with 21 valves placed in the aortic position. The sex ratio was 14 males: 29 females. In this group there were seven patients who tested positive by the Helisal test, representing 16.3% for the group. There was only one bleeder, representing 2.3% of this group and 14.3% of those who were tested positive for H. pylori. This only bleeder was anticoagulated for chronic atrial fibrillation.

Table 1 illustrates the same data but in accordance to age group. It is not surprising to note that the incidence of Helicobacter pylori...
ithromycin or amoxycillin and metronidazole) [22, 23].
and two antimicrobial agents (usually a combination of clar-
triple therapies of a proton-pump inhibitor (omeprazole)
in this association. However, many authorities reported very
scenario of further studies to demonstrate a cause and effect
were from the group of patients who tested positive for
patients who had symptoms of upper gastrointestinal bleed
significance.
(28.0% vs. 16.3%) although this failed to reach statistical
valve prosthesis when compared with bioprosthesis
frequency of positivity in patients with mechanical heart
valve prosthesis. There were no
demonstrate whether an association between the presence
of Helicobacter pylori infection and upper gastrointestinal bleed exists in this patient population. Chan and Woodruff
[21] report an incidence of upper gastrointestinal bleed of up
to 35% in a series of anticoagulated patients with disseminated
malignancy.
We found the incidence of Helicobacter pylori in patients
following heart valve surgery to follow the trend in the
general western population, namely an increased incidence
with age. Furthermore our study found a slightly increased
frequency of positivity in patients with mechanical heart valve prosthesis when compared with bioprosthesis
(28.0% vs. 16.3%) although this failed to reach statistical
significance.
A unique finding from the study was that the seven
patients who had symptoms of upper gastrointestinal bleed
were from the group of patients who tested positive for
Helicobacter pylori infection and were anticoagulated
because of mechanical valve prostheses. There were no
bleeders in those who were Helisal test negative irrespective of age, INR or position of the implant. This has important
implications in heart valve surgery as the mean age of the
general population is increasing together with an increased
incidence following heart valve surgery to follow the trend in the
Western society [19]. In the developing world the prevalence is
greatly in excess of this figure with over 80% of the people infected by the age of 50 [20]. The aim of this preliminary
study was to establish the incidence of upper gastrointestinal bleeding in patients following heart valve surgery and to
demonstrate whether an association between the presence of Helicobacter pylori infection and upper gastrointestinal bleed exists in this patient population. Chan and Woodruff
[21] report an incidence of upper gastrointestinal bleed of up
to 35% in a series of anticoagulated patients with disseminated
malignancy.
We found the incidence of Helicobacter pylori in patients
following heart valve surgery to follow the trend in the
general western population, namely an increased incidence
with age. Furthermore our study found a slightly increased
frequency of positivity in patients with mechanical heart valve prosthesis when compared with bioprosthesis
(28.0% vs. 16.3%) although this failed to reach statistical
significance.
A unique finding from the study was that the seven
patients who had symptoms of upper gastrointestinal bleed
were from the group of patients who tested positive for
Helicobacter pylori infection and were anticoagulated
because of mechanical valve prostheses. There were no
bleeders in those who were Helisal test negative irrespective of age, INR or position of the implant. This has important
implications in heart valve surgery as the mean age of the
general population is increasing together with an increased
likelihood of heart valve replacement in an older population. Unfortunately it is not immediately possible nor a likely
scenario of further studies to demonstrate a cause and effect
in this association. However, many authorities reported very
successful eradication rates of approximately 90% using
triple therapies of a proton-pump inhibitor (omeprazole)
and two antimicrobial agents (usually a combination of clar-
thromycin or amoxycillin and metronidazole) [22, 23].

4. Discussion
Helicobacter pylori infection has become the commonest
infection in humans with an incidence in the population
roughly equal to that of the patient’s age for the Western
society [19]. In the developing world the prevalence is
greatly in excess of this figure with over 80% of the people infected by the age of 50 [20]. The aim of this preliminary
study was to establish the incidence of upper gastrointestinal bleeding in patients following heart valve surgery and to
demonstrate whether an association between the presence of Helicobacter pylori infection and upper gastrointestinal bleed exists in this patient population. Chan and Woodruff
[21] report an incidence of upper gastrointestinal bleed of up
to 35% in a series of anticoagulated patients with disseminated
malignancy.
We found the incidence of Helicobacter pylori in patients
following heart valve surgery to follow the trend in the
general western population, namely an increased incidence
with age. Furthermore our study found a slightly increased
frequency of positivity in patients with mechanical heart valve prosthesis when compared with bioprosthesis
(28.0% vs. 16.3%) although this failed to reach statistical
significance.
A unique finding from the study was that the seven
patients who had symptoms of upper gastrointestinal bleed
were from the group of patients who tested positive for
Helicobacter pylori infection and were anticoagulated
because of mechanical valve prostheses. There were no
bleeders in those who were Helisal test negative irrespective of age, INR or position of the implant. This has important
implications in heart valve surgery as the mean age of the
general population is increasing together with an increased
likelihood of heart valve replacement in an older population. Unfortunately it is not immediately possible nor a likely
scenario of further studies to demonstrate a cause and effect
in this association. However, many authorities reported very
successful eradication rates of approximately 90% using
triple therapies of a proton-pump inhibitor (omeprazole)
and two antimicrobial agents (usually a combination of clar-
thromycin or amoxycillin and metronidazole) [22, 23].

In conclusion, the association between upper GI bleed and Helicobacter pylori infection in the presence of antico-
agulation is strong. Consequently we therefore propose that
all patients requiring heart valve surgery should be screened preoperatively and if patients are found to have Helicobacter pylori antibodies then they should proceed to the
establishment of active or chronic infection. If active
then this infection should be eradicated either before surgery is undertaken or immediately postoperatively. Similarly, patients found to have unexplained upper GI symptoms follow-
ing heart valve surgery should be screened for H. pylori and, if positive, to have this organism eradicated.

It is hoped that this simple, cheap and effective method of
detecting Helicobacter pylori will reduce the morbidity and
mortality associated with and not the consequent of the
anticoagulation following heart valve surgery.

References
1:1311–1315.
[8] Graham DY, Klein PD, Opekun AR, Bonton TW. Effect of age on the frequency of active Campylobacter pylori infection diagnosed by the
1873.
325:1127–1131.
[13] Landefeld CS, Beyth RJ. Anticoagulant related bleeding: clinical epi-
Appendix A . Conference discussion

Dr Pettersson (Copenhagen, Denmark): A very interesting paper and a convincing presentation. Should we take any consequences of these results?

Dr Liew: Certainly. I think that because it does produce a 25% incidence of GI bleed in those found to be H.P. positive, I think that the answer to your question is yes. I think that the first priority is for the elderly group of patients where we should establish a preoperative screening program, especially for those above 65 years of age. I think it also requires a multidisciplinary approach where by we enlist the help of our gastroenterology colleagues. Finally as there is very effective treatment, it should be treated with a stringent follow-up.

Dr Melo (Carnaxide, Portugal): I think this is very important information. Do your recommendations apply to other groups of patients, like valve patients that are not anticoagulated or old coronary patients?

Dr Liew: I have not done the studies on the coronary artery bypass graft patients. I think it is very important that as the incidence of H. pylori increases with age, that all patients above 65, regardless of whether they are having coronary or valve should be treated. I personally feel that everyone should have a Helicobacter pylori status determined prior to the surgical operation.