RESEARCH ARTICLE

Clinical statistical analysis of cholangiography robot

Rolly R. Tang*

School of Business, Xi'an International University, Xi'an, Shaanxi, China.

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This study mainly focused on the two major shortcomings of traditional cholangiography, namely the occupational exposure experienced by the operator and the postoperative complications of patients, and evaluated the results based on the incidence of postoperative complications and radiation dose under different conditions. The results indicated that the robot could efficiently and accurately perform cholangiography according to clinical requirements and could significantly avoid the operator being exposed to ionizing radiation. The cholangiography robot was able to successfully complete cholangiography and achieve good cholangiography effect, reduce postoperative complications, and eliminate professional exposure for doctors. To further verify the effectiveness and safety of the robot, based on previous research, this study compared the incidence of complications in robot treatment group and traditional treatment control group patients through clinical trials, and examined the difference in radiation dose between protected and unprotected areas. The results showed that the incidence of postoperative complications in the robot treatment group was significantly lower than that in the traditional treatment control group ($P < 0.01$). Therefore, robot treatment could be fully applied in clinical practice to replace traditional cholangiography modes, thereby improving the ability of cholangiography to assist in minimally invasive treatment of biliary diseases.

Keywords: cholangiography robot; effectiveness and safety; statistical analysis.

***Corresponding author:** Rolly R. Tang, School of Business, Xi'an International University, Xi'an, Shaanxi, China. Phone: +86 151 2920 8966. Email: happytrl@163.com.

Introduction

According to relevant data, there are 5 million liver and gallbladder surgeries performed annually in China, and approximately 80.75% of patients undergoing liver and gallbladder surgery require indwelling bile ducts to drain bile, who need to undergo cholangiography before extubation to realize the condition of the intrahepatic and extrahepatic bile ducts. Traditional cholangiography has two major drawbacks. The first one is that there are many unstable factors, and the incidence of postoperative complications in patients is high. When manually injecting contrast agents, it is difficult to maintain stable parameters such as contrast speed and radiation dose. The contrast effect also varies greatly depending on the operator's experience. There is a higher incidence of complications and adverse reactions after contrast injection. Clinical studies have shown that the incidence of adverse reactions after cholangiography in different medical facilities fluctuates between 5% and 23%. The causes of adverse reactions are not only due to the patient's own factors, but also mainly due to operational factors such as the speed of contrast agent injection, biliary pressure, and contrast

agent dosage. Researchers advocate using drip injection instead of push injection to reduce the pressure inside the biliary tract, thereby reducing the complications of traditional cholangiography [1]. However, this method leads to longer ionizing radiation time, and it is difficult to ensure that the contrast agent is filled into the intrahepatic bile duct, making it difficult to ensure the cholangiography effect [2]. The second disadvantage of traditional cholangiography is that the occupational exposure risk of operators is high. Bile duct contrast examination must be performed under X-ray fluoroscopy conditions with contrast agent being injected into the bile duct for real-time observation. For the operating doctor, each operation is an occupational exposure. Approximately one million patients require cholangiography every year. Previous studies have shown that, in a real radiation environment, although lead coatings of different thicknesses can block about 70% - 93% of radiation, they cannot completely block radiation, especially for exposed areas of the eyes and hands that medical personnel neglect to protect. Over time, this can cause skin damage, cataracts, and even cancer. Moreover, ionizing radiation damage is "linear without a threshold", and there is no safe dose for individuals. Consequently, due to occupational exposure and frequent postoperative adverse reactions of patients, operators inject a small amount of contrast agent in actual cholangiography operations to complete the cholangiography operation as quickly as possible. However, this operation often occurs in therapeutic procedures, such as percutaneous transhepatic biliary drainage (PTBD) or endoscopic retrograde cholangiopancreatography (ERCP). The instability of manual cholangiography leads to repeated cholangiography, often resulting in unclear or even masked lesions, which also greatly weakens the practical use of cholangiography and the precise diagnosis of biliary diseases. Therefore, it is necessary to improve existing technology, eliminate occupational exposure, ensure the accuracy and stability of cholangiography operations to effectively improve the quality of cholangiography diagnosis.

The bile duct cholangiography robot has improved traditional bile duct cholangiography. It is a specialized device for cholangiography, which uses automatic control technology to overcome the disadvantage of traditional control group cholangiography that can only rely on manual sensing and blind pushing. The use of this device completely avoids the professional exposure of doctors, and can accurately control the injection speed and amount, ensuring accurate and reliable cholangiography. Doctors can use this device to remotely control machine operations through the touch screen display on the remote-control end [3], monitor the pressure changes in the biliary tract in real time to ensure that the pressure in the patient's biliary tract is within a safe range during the injection process, reducing patient pain, and ensuring the safety of cholangiography by setting injection speed and pressure thresholds, and ensure good cholangiography results while eliminating occupational exposure issues for doctors [4]. The overpressure threshold alarm device ensures the safety of cholangiography operations, while providing real-time feedback on injection pressure [5]. Doctors can make preliminary judgments on the patient's condition based on this pressure value, and such data also provides reference for the evaluation of postoperative complications in patients [6]. Therefore, the successful development of cholangiography robot can be beneficial for solving the occupational exposure problem of operators, and its stable and accurate operational performance also ensures efficient and accurate cholangiography results. It can not only replace the operator in performing cholangiography, but also compensate for the shortcomings of traditional cholangiography.

This randomized controlled trial (RCT) clinical trial tested the application effect of cholangiography robot in real clinical environments by comparing the incidence of postoperative complications in patients and the

amount of ionizing radiation experienced by operators using a cholangiography robot for remote cholangiography examination and traditional cholangiography.

Materials and methods

Clinical trial case selection

The procedures of this clinical trial were approved by the Ethics Committee of the First Affiliated Hospital of Xi'an Jiaotong University (Xi'an, Shaanxi, China). All participants were required to sign informed consent forms. The clinical trial started on May 10th, 2023, and ended on August 16th, 2023. According to the principle of Intention-to-treat Analysis (ITTA), all enrolled subjects were analyzed [7, 8]. The original diseases suspected or diagnosed that required to perform this examination included gallstones in the biliary system, tumors in the biliary system, liver transplantation, and others (secondary surgery, after biliary intestinal anastomosis, *etc*.).

Experimental datasets

Full Analysis Set (FAS) referred to the analysis of all enrolled subject cases was employed in this study [9]. A total of 142 cases (including 1 missing case) was included in FAS dataset with 66 males and 75 females and the average age of 58.45 ± 13.93 years old. In addition, Per Protocol Set (PPS) referred to the analysis of all cases that comply with the trial protocol was constructed for the input of cases that had good compliance and completed the required information from the Case Report Form (CRF) with a total of 139 cases in PPS dataset [10]. Safety Analysis Set (SAS) referred to cases that had been enrolled and tested with safety baseline data including all randomized subjects who had received trial treatment) and at least once safety visit [11]. A total of 142 cases were included in SAS dataset. There were 2 dropped cases and 1 excluded case due to the lost follow up contact information for 2 dropped cases and failed cholangiography for 1 excluded case.

Comparison of robot and traditional cholangiography

Among the total of 141 compliance cases in FAS, 71 cases received robot cholangiography (experimental group) and 70 cases received traditional cholangiography (control group). The main indicators for post operation complications included fever, abdominal pain, jaundice, and other symptoms that occurred 3 days after operation. The cholangiography effects were divided into 5 different grades with grades 1-3 showing no or incomplete visualization of the common bile duct and its lower end, left and right hepatic ducts, grades 4-5 showing clear branching of the common bile duct and its lower end, left and right hepatic ducts, and intrahepatic bile ducts [12]. For the safety evaluation and occupational exposure (radiation dose) comparison, mechanical safety, electrical safety, ionizing radiation safety, and equipment system security were compared between the two groups.

Statistical analysis

Power Analysis and Sample Size (PASS), version 15 (NCSS, LLC., Kaysville, Utah, USA) was employed in this RCT study. The bilateral 95% Clopper Pearson (CI) was calculated using either the binomial distribution based single sample rate exact probability method or the Score (Wilson) method with the FAS and PPS datasets to analyze whether the compliance rate between clinical cholangiography quality and clinical diagnostic requirements was higher than the target value of 90% [13]. Further, non-parametric Chi-square tests were conducted on the main indicator comparison [14]. If the expected frequency of an indicator was less than 5, Fisher's exact test was required. For the degree of occupational exposure (radiation dose), t-tests of parametric tests were used to perform normality tests that the exposure of operator to radiation dose were measured using log, and ln X or SQRT was used to convert it to a normal distribution. Further bilateral t-tests were used for intergroup comparison between experimental group and control group [15]. The *P* value less than 0.05 was

Table 1. Compliance rate of clinical cases.

Data set	Compliance cases (total)	Coincidence rate	Accurate 95% CI
FAS	141 (142)	99.30%	96.1% - 100%
PPS	139 (141)	98.60%	95% - 99.8%
Extreme*	139 (142)	97.90%	94% - 99.6%

Note: * The most conservative scenario, where all excluded subjects were considered as not meeting clinical diagnostic requirements.

Table 2. Comparison of cholangiography results between groups.

Group	No complications (rate)	Incidence of complications (rate)	Total
Control Group	52 (73.24%)	19 (26.76%)	71
Treatment Group	64 (91.43%)	6 (8.57%)	70
Total	116 (82.26%)	25 (17.73%)	141

defined as a significant difference and *P* less than 0.01 as very significant difference.

Results and discussion

Compliance of clinical cases

Double sided 95% CI was calculated using either the binomial distribution based single sample exact probability method or the Score (Wilson) method based on FAS and PPS, respectively [16]. The lower limit of the confidence interval was set as no less than 90%, which would make the compliance rate reach the target. The compliance rate between clinical cholangiography quality and clinical diagnostic requirements was analyzed to investigate if it was higher than the target value of 90% (Table 1).

Incidence rate of complications

Statistical analysis was conducted on both groups to inspect whether there were complications after the cholangiography. Among the total 141 cases, 52 cases and 64 cases were no complications after the operation in the control and experimental groups, respectively, with a rate of 73.24% and 91.43%. There were 19 cases of complications in the control group with a complication rate of 26.76%, and 6 cases of complications in the experimental group with a complication rate of 8.57% (Table 2). The incidence of complications in the control group was much higher than that in the experimental group ($P < 0.01$), indicating a significant reduction in the incidence of postoperative complications in patients using robot cholangiography.

Comparison of cholangiography effects

The classification of cholangiography effects showed that there were 13 cases in the control group within the grades 1-3, accounting for 18.31% of all cases in this group, while 58 cases within grades 4-5 including 43 cases in grade 4 and 15 cases in grade 5, accounting for 81.69% of the whole group. The experimental group had a higher proportion of cholangiography results in grades 4-5 than that in the control group with 65 cases in grades 4-5 including 37 cases in grade 4 and 28 cases in grade 5, accounting for 92.86% of the enrolled cases in the group ($P < 0.05$). The number of cases in grades 1-3 in experimental group was also significantly lower than that in the control group with only 5 cases accounting for 7.14% of the entire group (Table 3). The results suggested that the cholangiography effect of experimental group was significantly improved compared to control group [17], and further proved that the experimental group had a significantly improved contrast effect compared to the control group. The proportion of contrast enhancement in the common bile duct and its lower end, left and right hepatic ducts, and intrahepatic bile ducts was significantly higher than that in the control group ($P < 0.05$). This

Table 3. Cholangiography effect grading.

Group	Grades 1 - 3	Grades 4 - 5	Total
Control group	13 (18.31%)	58 (81.69%)	71
Experimental group	5 (7.14%)	65 (92.86%)	70
Total	18	123	141

Table 4. Radiation doses under different conditions.

Group	Number of cases	Radiation dosage (μSv, mean ± SD)	Median (min - max)
Protection Zone	141	1.27 ± 0.75	1.03 (0.19 - 4.24)
Unprotected Zone	141	60.35 ± 45.19*	50.00 (10 - 230)

Note: * very significantly different from the protected zone ($P < 0.01$).

phenomenon might be caused by the difficulty in controlling the injection speed, biliary pressure, and dosage during the manual pushing process. The increase in biliary pressure during the manual pushing of contrast agents might also cause bile to reflux from the biliary system into the bloodstream, and if bacteria were present in the bile, bile duct venous or lymphatic reflux might lead to systemic bacteremia, which was not monitored by traditional cholangiography. On the other hand, the infusion speed of the cholangiography robot was constant without sudden changes of injection speed or pressure. Further, the robot used pressure sensors to accurately measure the injection pressure and displayed it in real-time on the touch panel of the control terminal, which made doctors can preliminarily judge the patient's status based on the cholangiography situation and adjust the speed and pressure appropriately, thereby reducing the incidence of complications.

Exposure of radiation dosage

The differences of both groups in radiation exposure to operators under protected and unprotected areas during the cholangiography process were shown in Table 4. The radiation dose received by clinical doctors in protected area during cholangiography injection was 1.27 ± 0.75 μSv, while the radiation dose received in unprotected zone was 60.35 ± 45.19 μSv. The results indicated that the radiation level in the protected zone was much lower than that in the unprotected zone ($P < 0.01$). However, the results also reflected from another perspective that, even under protective measures, the body of clinical doctors were still exposed to a certain amount of radiation. During the examination process, the unprotected exposed areas including maxillofacial region, arm skin, and eyes of the operating doctor were exposed to a large amount of radiation. Wearing lead protection clothing could significantly reduce the radiation dosage in protected areas. However, there was still a certain amount of radiation exposure in the protected zone. Therefore, simple protection could not eliminate occupational exposure problems, and heavy lead clothing undoubtedly increased the workload of operators, affected operations, and even brought other operational difficulties. The results suggested that remote-controlled robot cholangiography might be the solution to completely avoid the radiation exposure of the operation doctors.

Safety evaluation

The safety evaluation (SAS) was performed mainly based on mechanical safety, electrical safety, ionizing radiation safety and equipment system safety of the cholangiography injection system [18]. There were no significant differences between the two groups among the four safety categories.

This clinical trial tested the application effect of cholangiography robot in real clinical

environments. The results indicated that the equipment could efficiently and accurately perform cholangiography according to clinical requirements and significantly avoid the operator being exposed to ionizing radiation. It not only replaced the operator in performing cholangiography manually, but also compensated for the shortcomings of traditional cholangiography including occupational exposure experienced by the operator and the postoperative complications of patients. The successful development of cholangiography robot was not only beneficial for solving the occupational exposure problem of operators, but its stable and accurate operational performance also ensured efficient and accurate cholangiography results. The results confirmed that cholangiography robot could be fully applied in clinical practice to replace traditional cholangiography modes, thereby improving the ability of cholangiography to assist in minimally invasive treatment of biliary diseases. However, the medical record information collected in this study was relatively simple, and further studies should include more cases to explore the setting of cholangiography parameters for different diseases and develop personalized and standardized new models for cholangiography.

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