Transactions on Materials, Biotechnology and Life Sciences
ISSN: 2960-1932, eISSN: 2960-2319 | Volume 3
BLSME 2024

Sample Size Estimation and Statistical Analysis of Cholangiography Robots

Rongli Tang *

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

* Corresponding author: happytrl@163.com

Abstract. In recent years, with the continuous innovation of medical devices encouraged by the government and the investment and attention of enterprises in research and development, coupled with the relevant requirements of the CDE (Center for Drug Evaluation) of the National Medical Products Administration, in order to improve the efficiency of trials and accelerate the launch of cholangiography robots, medical device research and development enterprises are increasingly focusing on the design of clinical trial plans, adopting more scientific, reliable, efficient and standardized statistical designs. Insufficient sample size may lead to issues with sample representativeness, while human centered trials are very expensive, and excessive sample size could increase the difficulty of clinical research. Therefore, this study used the "golden rule" of RCT (Randomized Controlled Trials), combined with the outcome indicators, test level, confidence, dropout rate, etc., to estimate the number of cases in the clinical efficacy comparison study of the cholangiography robot.

Keywords: sample size; statistical analysis; cholangiography robot.

1. The Necessity of Estimating Sample Size

When the sample size is insufficient, we cannot rule out the influence of accidental factors, if a negative result appears, it cannot be determined whether the difference itself does not exist or the testing efficiency is insufficient? However, when the sample size is too large, it will increase the difficulty of clinical research. Therefore, selecting an appropriate sample size can ensure that clinical experiments obtain scientific, truthful, and reliable conclusions while making the research feasible.

According to existing relevant literature, the main outcome indicators of adverse reactions after remote cholangiography are the Incidence Rate of Complications, the Degree of Occupational Exposure of Operators (Radiation Dosage), and the secondary indicators are the Hydraulic Detection Value, Cholangiography Speed, and the Injection Dose of Contrast Agent. Besides, the Incidence Rate of Complications is categorical variable, and other indicators are continuous variables.

2. Statistical design

According to the recognized PICOS principles in clinical research, the statistical design of this study is:

(1) The research subject Population (P) is a patient with partial indwelling biliary drainage in the liver and gallbladder surgery department;

(2) Intervention (I) refers to the treatment measures or exposure factors of concern;

(3) Control measure (C) is not using remote cholangiography equipment;

(4) The outcome indicator (O) is the diagnostic and therapeutic effect of the intervention measures. In this study, the main observed outcome indicators are the incidence of adverse reactions after contrast imaging and the degree of occupational exposure experienced by the operator;

(5) Study Design Type (S) is a randomized controlled trial (RCT) with parallel design.

3. Methods and analytical procedures

This clinical trial adopts a single center, prospective, randomized controlled clinical trial. Obtain the Incidence Rate of Complications in two groups after contrast surgery, and set the test level (probability of first type error) α=0.025 unilateral, test efficacy (confidence) 1- β=85% for unilateral non-parametric testing for χ^2 (Chi-Square Test), set the ratio of the number of cases between the treatment group and the control group to be 1:1. For the other 4 indicators (Radiation Dosage, Hydraulic Detection Value, Cholangiography Speed, and the Injection Dose of Contrast Agent), obtain the mean and standard deviation of two groups, set the testing level (probability of first type error) α=0.025 unilateral, test efficacy (confidence) 1- β=99% for bilateral T-test, with 1:1 ratio of cases in the treatment and control groups.

Based on the above parameters, use PASS 15 (Power Analysis and Sample Size Software) to calculate Sample Size Group 1 (N1), which means how many study subjects need to be included in the control group, and Sample Size Group 2 (N2), which means how many study subjects need to be included in the treatment group, in order to obtain the required sample size for the treatment group and the control group.

4. Sample size and its determination basis

4.1. Incidence Rate of Complications

The study was designed as a Randomized Controlled Trial (RCT), with the outcome measure being the incidence of adverse reactions as a categorical variable. According to the preliminary trial results, the incidence of complications in the treatment group was 10/250=4%, while according to previous literature reports, the incidence of complications in the placebo control group was 20%.

4.1.1. Z-Test (Unpooled)

On one side non-parametric χ^2 (chi-square test), when estimating standard errors, the test type is Z-Test (Unpooled), and the two sample rates are not averaged and merged.

Numeric Results for Testing Two Proportions using the Z-Test with Unpooled Variance.

H0: P1 - P2 $\geq$ 0 vs. H1: P1 - P2 = D1 < 0.

Table 1. Tests for Two Proportions

Target Power	Actual Power*	N1	N2	N	P1	P2	Diff D1	Alpha
0.85	0.85158	56	56	112	0.04	0.20	-0.16	0.05

* Power was computed using the normal approximation method.

This parallel randomized controlled study consists of a treatment group using equipment and a control group using manual methods, the Incidence Rate of Complications is the primary outcome measure to be observed, and the testing level is α= 0.05 (unilateral), test efficacy is 1- β= 0.85, use PASS 15 to calculate the required sample size N1=N2=56 cases for the treatment group and control group.

Table 2. Dropout-Inflated Sample Size

Dropout Rate	Sample Size			Dropout-Inflated Enrollment Sample Size			Expected Number of Dropouts		
	N1	N2	N	N1'	N2'	N'	D1	D2	D
10%	56	56	112	63	63	126	7	7	14

Assuming dropout rate is 10% for the research object, the corrected sample size N1=N2=63 cases, which means that the treatment group needs to include 63 subjects and the control group needs to include 63 subjects, achieving an efficiency of 85.158%.

4.1.2. Z-Test (Pooled)

On one side non-parametric χ^2 (chi-square test), when estimating standard errors, the test type is Z-Test (Pooled), and the two sample rates are merged and averaged.

Table 3. Two-Sample T-Tests Assuming Equal Variance

Target Power	Actual Power*	N1	N2	N	P1	P2	Diff D1	Alpha
0.85	0.85050	58	58	116	0.04	0.20	-0.16	0.05

* Power was computed using the normal approximation method.

Using PASS 15, the required sample size N1=N2=58 cases for the treatment and control groups was calculated. Assuming dropout rate is 10% for the research object, the corrected sample size N1=N2=65 cases, which means that the treatment group needs to include 65 subjects, and the control group needs to include 65 subjects, achieving an efficiency of 85.050%.

4.2. Radiation Dosage

Next, in order to further reduce the ionizing radiation of operating doctors and eliminate their occupational exposure, we explored whether remote cholangiography has advantages? The study was designed as a parallel Randomized Controlled Trial (RCT), with the main outcome measure being the continuous variable, namely the radiation dose in the lead Unprotected area and the lead protected area.

4.2.1. Radiation Dose in Unprotected Zone

According to the preliminary test results, it is estimated that the single radiation dose in the unprotected area of the control group is about (3.72 ± 2.02) μSv, now we are exploring whether using remote-controlled cholangiography equipment to complete cholangiography can reduce the ionizing radiation of the operating doctor and avoid exposing the operating doctor to X-ray radiation compared to the unprotected area of lead clothing? Among them, the inspection level α= 0.05 (bilateral), test efficacy 1- β= 0.99, therefore, the required sample size N1=N2=22 cases for the treatment group and control group were calculated using PASS 15 software.

Table 4. Two-Sample T-Tests Assuming Equal Variance

Target Power	Actual Power	N1	N2	N	μ1	μ2	δ	σ	Alpha
0.99	0.99184	22	22	44	3.72	1.00	2.72	2.02	0.05
0.99	0.99037	52	52	104	3.72	2.00	1.72	2.02	0.05
0.99	0.99016	291	291	582	3.72	3.00	0.72	2.02	0.05

Assuming dropout rate is 10% for the study subjects, the corrected sample size N1=N2=25 cases, which means that 25 subjects need to be included in each group, achieving a 99.184% efficiency.

4.2.2. Radiation Dose in Lead Suit Protection Zone

Based on the preliminary test results, it is estimated that the radiation dose in the control group's protective zone is approximately (0.19 ± 0.15) per dose μSv, now we are exploring whether using remote-controlled cholangiography equipment to complete cholangiography can reduce the ionizing radiation of the operating doctor and avoid exposing the operating doctor to X-ray radiation compared to the lead suit protection zone? Among them, the inspection level α= 0.05 (bilateral), test efficacy 1- β= 0.99, therefore, the required sample size N1=N2=24 cases for the treatment group and control group were calculated using PASS 15 software.

Table 5. Two-Sample T-Tests Assuming Equal Variance

Target Power	Actual Power	N1	N2	N	μ1	μ2	δ	σ	Alpha
0.99	0.99022	24	24	48	0.19	0.00	0.19	0.15	0.05

Assuming dropout rate is 10% for the study subjects, the corrected sample size N1=N2=27 cases, which means that each group needs to include 27 subjects, achieving a 99.022% efficiency.

4.3. Hydraulic Detection Value

The pressure change in the biliary tract during contrast agent injection is an important indicator that affects the incidence of postoperative adverse reactions in patients. This indicator is subdivided into three observation outcome indicators: human intrahepatic bile duct hydrostatic pressure, extrahepatic bile duct pressure, and Oddi sphincter pressure, the specific calculation process is as follows.

4.3.1. Hydrostatic Pressure of Intrahepatic Bile Duct

Based on the preliminary test results, it is estimated that the hydrostatic pressure of the intrahepatic bile duct in the control group is (2.79 ± 0.212) kPa. Now, we explore whether reducing the hydrostatic pressure of the intrahepatic bile duct can reduce the adverse reactions of patients after contrast surgery? The smaller the static water pressure of the intrahepatic bile duct, the lower the proportion of patients with adverse reactions after angiography? Among them, the inspection level α= 0.05 (bilateral), test efficacy 1- β= 0.99, therefore, the required sample size N1=N2=2 cases for the treatment group and control group were calculated using PASS 15 software.

Table 6. Two-Sample T-Tests Assuming Equal Variance

Target Power	Actual Power	N1	N2	N	μ1	μ2	δ	σ	Alpha
0.99	0.99980	2	2	4	2.790	0.000	2.790	0.212	0.05
0.99	1.00000	3	3	6	2.790	1.000	1.790	0.212	0.05
0.99	0.99089	4	4	8	2.790	2.000	0.790	0.212	0.05

Assuming dropout rate is 10% for the study subjects, a corrected sample size of N1=N2=3 cases, each group needs to include 3 subjects, achieving a 99.980% efficiency.

4.3.2. Extrahepatic and Intrahepatic Bile Duct Pressure

Based on the preliminary test results, it is estimated that the extrahepatic bile duct pressure in the control group is (1.175 ± 0.276) kPa. Now, we explore whether reducing extrahepatic bile duct pressure can reduce adverse reactions in patients after contrast surgery? The lower the pressure inside the extrahepatic bile duct, the lower the proportion of patients with adverse reactions after angiography? Among them, the inspection level α= 0.05 (bilateral), test efficacy 1- β= 0.99, therefore, the required sample size N1=N2=4 cases for the treatment group and control group were calculated using PASS 15 software.

Table 7. Two-Sample T-Tests Assuming Equal Variance

Target Power	Actual Power	N1	N2	N	μ1	μ2	δ	σ	Alpha
0.99	0.99841	4	4	8	1.175	0.000	1.175	0.276	0.05
0.99	0.99039	93	93	186	1.175	1.000	0.175	0.276	0.05

Assuming dropout rate is 10% for the study subjects, a corrected sample size of N1=N2=5 cases, each group needs to include 5 subjects, achieving a 99.841% efficiency.

4.3.3. Oddi Sphincter Pressure

Based on the preliminary test results, it is estimated that the pressure of the Oddi sphincter in the control group is (1.27 ± 0.283) kPa. Now, we explore whether reducing the pressure of the Oddi sphincter can reduce the adverse reactions of patients after angiography? The lower the pressure on the Oddi sphincter, the lower the proportion of patients with adverse reactions after angiography? Among them, the inspection level α= 0.05 (bilateral), test efficacy 1- β= 0.99, therefore, the required sample size N1=N2=4 cases for the treatment group and control group were calculated using PASS 15 software.

Table 8. Two-Sample T-Tests Assuming Equal Variance

Target Power	Actual Power	N1	N2	N	μ1	μ2	δ	σ	Alpha
0.99	0.99932	4	4	8	1.27	0.00	1.27	0.283	0.05
0.99	0.99087	42	42	84	1.27	1.00	0.27	0.283	0.05

Assuming dropout rate is 10% for the study subjects, a corrected sample size of N1=N2=5 cases, each group needs to include 5 subjects, achieving a 99.932% efficiency.

4.4. Cholangiography Speed

This study is parallel Randomized Controlled Trial (RCT). The treatment group underwent cholangiography using a remote-controlled cholangiography device, while the control group underwent manual cholangiography, continuous variable imaging speed was the main outcome measure observed.

Table 9. Two-Sample T-Tests Assuming Equal Variance

Target Power	Actual Power	N1	N2	N	μ1	μ2	δ	σ	Alpha
0.99	0.99001	241	241	482	0.71	0.80	-0.09	0.23	0.05
0.99	0.99018	55	55	110	0.71	0.90	-0.19	0.23	0.05
0.99	0.99196	25	25	50	0.71	1.00	-0.29	0.23	0.05

Based on the preliminary test results, it is estimated that the contrast imaging speed of the control group is (0.71 ± 0.23) ml/s. Now, we explore whether increasing the contrast imaging speed can reduce the adverse reactions of patients after contrast surgery? The faster the imaging speed, the lower the proportion of patients with adverse reactions after imaging surgery? Among them, the inspection level α= 0.05 (bilateral), test efficacy 1- β= 0.99, therefore, the required sample size N1=N2=25 cases for the treatment group and control group were calculated using PASS 15 software.

Assuming dropout rate is 10% for the study subjects, the corrected sample size N1=N2=28 cases, which means that 28 subjects need to be included in each group, achieving a 99.196% efficiency.

4.5. The Injection Dose of Contrast Agent

The treatment group underwent cholangiography using a remote-controlled cholangiography device, while the control group underwent manual cholangiography, the amount of contrast agent injected was the main outcome measure to be observed.

Table 10. Two-Sample T-Tests Assuming Equal Variance

Target Power	Actual Power	N1	N2	N	μ1	μ2	δ	σ	Alpha
0.99	0.99123	34	34	68	23.98	10.00	13.98	13.10	0.05
0.99	0.99007	399	399	798	23.98	20.00	3.98	13.10	0.05
0.99	0.99001	175	175	350	23.98	30.00	-6.02	13.10	0.05
0.99	0.99094	26	26	52	23.98	40.00	-16.02	13.10	0.05
0.99	0.99315	11	11	22	23.98	50.00	-26.02	13.10	0.05

According to the preliminary test results, it is estimated that the injection dose of contrast agent in the control group is (23.98 ± 13.10) kPa, and the injection dose of contrast agent is not a risk factor for postoperative adverse reactions. Therefore, the sample size required for the treatment group and the control group calculated using PASS 15 software is only used as a reference for the above results.

Similarly, the dropout rate of the study subjects is 10%, and the corrected sample size is also only used as a reference for the above results.

5. Summary

We calculated the sample size required for the following five outcome indicators: the incidence rate of complications of remote cholangiography, the degree of occupational exposure of operators, the hydraulic detection value, the imaging speed, and the injection dose of contrast agent, the summary is as follows.

Table 11. Summary of sample size required for remote cholangiography

Main Indicators	Secondary Indicators	Dropout Rate	Treatment Group	Control Group	Total	Actual TE
Incidence Rate of Complications	Z-Test (Unpooled)		56	56	112	85.158%
		10%	63	63	126	
	Z-Test (Pooled)		58	58	116	85.050%
		10%	65	65	130	
Radiation Dosage	Unprotected		22	22	44	99.184%
		10%	25	25	50	
	Protection		24	24	48	99.022%
		10%	27	27	54	
Hydraulic Detection Value	Intrahepatic		2	2	4	99.980%
		10%	3	3	6	
	Extrahepatic		4	4	8	99.841%
		10%	5	5	10	
	Oddi		4	4	8	99.932%
		10%	5	5	10	
Cholangiography Speed			25	25	50	99.196%
		10%	28	28	56	
The Injection Dose of Contrast Agent			For reference only			

From the above analysis results, we can draw the following conclusions.

First, there are multiple outcome indicators in the study, we focus on the incidence rate of complications and the degree of occupational exposure. Second, the sample number of incidence rate of complications is the largest. Finally, for the main outcome indicator of incidence rate of complications χ^2 (chi-square test), when estimating the standard error, an efficiency of 85.158% can be achieved without average merging of two sample rates, while an efficiency of 85.050% can be achieved with average merging of two sample rates, the former has slightly higher testing efficiency.

In summary, considering the dropout rate, the minimum required sample size for the RCT treatment group and control group is 63 cases respectively, which means that the minimum required sample size for the experiment is 126 subjects.

Acknowledgements

This research was supported by Xi'an Science and Technology Bureau Science and Technology Plan Funds (22GXFW0109) and Key R&D Plan of Shaanxi Province Funds (2021GXLH-Z-004).

References

[1] Kwok J Y Y, Kwan J C Y, Auyeung M, et al. Effects of mindfulness yoga vs stretching and resistance training exercises on anxiety and depression for people with Parkinson disease: a randomized clinical trial [J]. JAMA neurology, 2019, 76 (7): 755 - 763.

[2] Shaygan M, Yazdani Z, Valibeygi A. The effect of online multimedia psychoeducational interventions on the resilience and perceived stress of hospitalized patients with COVID-19: a pilot cluster randomized parallel-controlled trial [J]. BMC psychiatry, 2021, 21 (1): 1 - 12.

[3] Du H, Lian Z, Lan L, et al. Application of statistical analysis of sample size: How many occupant responses are required for an indoor environmental quality (IEQ) field study[C]//Building Simulation. Beijing: Tsinghua University Press, 2023, 16 (4): 577 - 588.

[4] Kappos L, Fox R J, Burcklen M, et al. Ponesimod compared with teriflunomide in patients with relapsing multiple sclerosis in the active-comparator phase 3 OPTIMUM study: a randomized clinical trial [J]. JAMA neurology, 2021, 78 (5): 558 - 567.

[5] Serdar C C, Cihan M, Yücel D, et al. Sample size, power and effect size revisited: simplified and practical approaches in pre-clinical, clinical and laboratory studies [J]. Biochemia medica, 2021, 31 (1): 27 - 53.

[6] Hennink M, Kaiser B N. Sample sizes for saturation in qualitative research: A systematic review of empirical tests [J]. Social science & medicine, 2022, 292: 114523.

[7] Baeza-Delgado C, Cerdá Alberich L, Carot-Sierra J M, et al. A practical solution to estimate the sample size required for clinical prediction models generated from observational research on data[J]. European Radiology Experimental, 2022, 6 (1): 22.

[8] Ugwuanyi L T, Ede M O, Agbigwe I B, et al. Effect of rational emotive behaviour therapy on depressive symptoms in a sample of parents of children with intellectual disability [J]. Journal of Rational-Emotive & Cognitive-Behavior Therapy, 2023, 41 (1): 128 - 143.

[9] Marso S P, Daniels G H, Brown-Frandsen K, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes[J]. New England Journal of Medicine, 2016, 375 (4): 311 - 322.

[10] Gerçeker G Ö, Bektaş M, Aydınok Y, et al. The effect of virtual reality on pain, fear, and anxiety during access of a port with huber needle in pediatric hematology-oncology patients: Randomized controlled trial [J]. European Journal of Oncology Nursing, 2021, 50: 101886.