Original Article

Performance in 6-min walk test in prediction of post-operative pulmonary complication in major oncosurgeries: A prospective observational study

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ABSTRACT

Background and Aims: Post-operative pulmonary complications (PPC) contribute to increased morbidity and mortality, necessitating pre-operative functional assessment. Six-minute walk test (6MWT) is a simple option for functional assessment. **Methods:** This is a prospective observational study conducted in 75 patients who underwent elective abdominal or thoracic oncosurgery under general anaesthesia with either age above 60 years or with cardiopulmonary diseases or obstructive sleep apnoea or low serum albumin or smoking. Patients with history of acute coronary syndrome in past 6 months, dyspnoea at rest, severe pain, inability to walk or interpret instructions and haemodynamic instability were excluded. Preoperatively 6MWT was conducted according to the American Thoracic Society guidelines and patients were observed for PPC. Patients were divided into two groups: group 1–no PPC and group 2–developed PPC. Statistical analysis was done using SPSS software (version 11.0.1). Categorical variables were assessed using Chi-square/Fisher's exact test and continuous variables using student's t-test/Mann-Whitney U test. Association was tested using logistic regression. **Results:** Out of the 75 patients, 40 patients had no PPC (group 1) and 35 patients had PPC (group 2) including a death. The 6MWD of group with PPCs was significantly less (344 ± 61.927 m) compared to the group without PPCs (442.28 ± 83.194 m, *P* value = 0.001). The cut-off 6MWD obtained was 390 m, which correlated with longer duration of hospital stay and ICU stay (*P* = 0.001). **Conclusion:** Six-minute walk test is a reliable predictor of post-operative pulmonary complications with a cut-off 6MWD of 390 m in the studied oncosurgery patients.

Key words: Exercise test, oncosurgery, perioperative care, post-operative complications, prospective studies, walk test

INTRODUCTION

Six-minute walk test (6MWT) was introduced in 1982 for pulmonary evaluation mostly after lung resection surgeries.[1] It is easy to perform, inexpensive and does not need special equipment or trained personnel, hence recently being included in pre-operative evaluation.[2] This gives an assessment of tolerance of daily activities.[1] Oncology patients have several overlapping factors interfering with exercise capacity and multiple risk factors for post-operative pulmonary complications.[3] Changes to the respiratory system occur immediately under general anaesthesia.[3,4]

Pulmonary evaluation methods in pre-operative period for those at risk are mainly spirometry evaluation of lung function tests (PFT) and the standard method is cardiopulmonary exercise testing (CPET).[5] The PFT

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reports are often not reliable as it is influenced by interpretation and patient performance, while CPET is a complex procedure requiring specialised equipments and expertise. Hence, alternative methods of functional capacity assessment like 6MWT, incremental shuttle walk test and stair-climbing test are sought for.

Our aim was to assess the relationship of 6-min walking distance (6MWD) with post-operative pulmonary complications (PPC) among patients appearing for major oncosurgery. Primary objective was to correlate 6MWD with occurrence of PPC. Secondary objectives were to find association of 6MWD with length of hospital stay and to find the association of PPC with risk factors like smoking, serum albumin, PFT findings as well as with variations in haemodynamic parameters which include blood pressure (BP), heart rate (HR) and oxygen saturation (SpO_2). The mean 6MWD can vary between different ethnic groups requiring need of a study in our patient population.[6]

METHODS

This is a prospective observational study conducted at the Regional Cancer Centre (RCC), Thiruvananthapuram. Institutional review board (IRB NO: 11/2016/16) and hospital ethics committee (HEC NO: 27/2016) approval was obtained prior to starting the study.

Study population included all patients undergoing elective thoracic or abdominal surgery of probable duration ≥3 h under general anaesthesia in the RCC, Thiruvananthapuram during the period March 2017–February 2018 with at least any one of the following criteria: age more than 60 years, history of cardiovascular or pulmonary diseases, serum albumin ≤30 g/L, chronic smoker and chest X-ray with abnormal lung parenchymal/chest wall findings.[4] Exclusion criteria were patients who had unstable angina/myocardial infarction/acute coronary syndrome in the previous 6 months, dyspnoea at rest, inability to walk (orthopaedic problems, cerebrovascular accidents, balance disorders), severe pain, unable to interpret or follow instructions, and resting tachycardia (HR ≥120 beats per min)/uncontrolled hypertension (BP ≥180/100 mm of Hg).[1]

As per the institutional protocol, all patients underwent the routine pre-operative evaluation. Patients who satisfied the inclusion criteria were selected and explained about the test procedure. Patients were instructed to walk at their comfortable pace back and forth in the marked track with turn-around at either end for a duration of 6 min and were informed that they will be allowed to take rest or stop the test in case of discomfort. Eighty patients who were willing were included after obtaining informed written consent. Five patients were excluded due to change in treatment plan. The remaining 75 patients were enrolled and underwent the 6MWT preoperatively.

We conducted the test in a flat, straight hallway 25 metres long, near our pre-anaesthesia clinic block or near surgical ward after admission, where emergency assistance was available along with defibrillator and emergency cart. Test was conducted by the first author who was trained in cardiopulmonary resuscitation. A stop watch, measuring tape, portable pulse oximetry probe, sphygmomanometer and lap counter were used as per the ATS guidelines.[1] The test was stopped if patient experienced any chest pain, intolerable dyspnoea, leg cramps, diaphoresis, pale or ashen appearance and medical assistance was given. Before and after the test, the patient's blood pressure (BP), heart rate (HR), oxygen saturation (SpO_2) and Borg dyspnoea scores [Table 1] were noted down on the proforma.[7] Further, the patients underwent surgery as planned under general anaesthesia plus epidural anaesthesia according to our routine protocols and received the routine post-operative care and multimodal analgesia including epidural analgesia. The occurrence of pulmonary complications during post-operative period was noted down until discharge from the hospital.[8] The patients were divided into two groups based on occurrence of PPC: group 1–No PPC

Table 1: Borg Rating of Perceived Exertion

#	Level of Exertion
6	No exertion at all
7	
7.5	Extremely light (7.5)
8	
9	Very light
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard (heavy)
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

Courtesy: Bmjopensem.bmj.org; # – score

and group 2–with PPC. The PPC observed included the following; Prolonged mechanical ventilation >48 hrs, Atelectasis (radiological diagnosis), Bronchitis, Bronchospasm, acute respiratory distress syndrome (ARDS) by the Berlin criteria, Pneumonia, Exacerbation of chronic lung disease, Respiratory failure.[8,9]

Difference in 6MWD, pre and post-test haemodynamic parameters, dyspnoea scores and other risk factors were compared between these groups. Association of risk factors with PPC was also studied.

Statistical analysis was done using SPSS 11.0.1. A sample size of 15 cases in the PPC group and 60 cases in the non-PPC group was assumed to be required in order to detect a difference higher than 100 m of 6MWD between groups, expecting an incidence of PPC 20%, standard deviation (SD) of 100 m assuming alpha error = 5%, 80% power of detection based on the study by Keeratichananont *et al*.[5] Hence, a total sample size of 75 was taken. The categorical variables were represented using frequency and percentage. Continuous variables were reported using mean and SD. The significance between two categorical variables was assessed using Chi-square/Fisher's exact test. For continuous variables, normality was tested and for those satisfying normality, student's *t*-test was done. For non-normal variables, Mann–Whitney U test was done. A *P* value less than 0.05 considered to be significant. Association was tested using logistic regression.

RESULTS

The study included 75 oncology patients who underwent thoracic and abdominal oncosurgery in our tertiary cancer care centre under general anaesthesia with duration more than or equal to 3 h. There were no missing data. All the patients completed the test without any complications. Among the study group, 54 were males and 21 patients were females. Mean age of the study population was 60.5 ± 9.63 years, 13 patients were more than 70 years old, 22 were between 50 and 70 years and 10 patients were below 50 years of age. No significant association was found for gender and PPC (P = 0.680). Among them, 35 patients (46.7%) had PPC with one death due to pulmonary thromboembolism. Pneumonia was the most commonly observed post-operative pulmonary complication in the study group (22 patients out of 35). Other PPC were respiratory failure (4/35), atelectasis (4/35), bronchospasm (3/35), bronchitis (1/35) and ARDS (1/35).

Sixtyseven out of 75 patients belonged to ASA class one and two while eight patients were of ASA class three. The patients categorised as ASA class above two had more risk for PPC compared to class equal to or below two (OR = 9.750, 95% CI = 1.135–83.769, P = 0.038). Seventy patients in our group belonged to the non-dependent group (ECOG 0). Five patients were of ECOG 2 performance status. Among the patients enrolled, 58% were non-smokers. Among the 32 smokers, 26 people had smoking history with more than 20 pack-years.

According to the occurrence of PPC, the patients were divided into 2 groups: Group 1 (patients without PPC) and Group 2 (patients with PPC). The 6MWD and comorbidities were compared for the two groups [Figure 1].

No significance was found for age, BMI, smoking history and serum albumin between the two groups. Spirometry finding forced expiratory volume (FEV1) had a mean value of 76.63% of predicted with only borderline significance (P = 0.048); FVC was significant with mean 74.11% of predicted (P = 0.009).

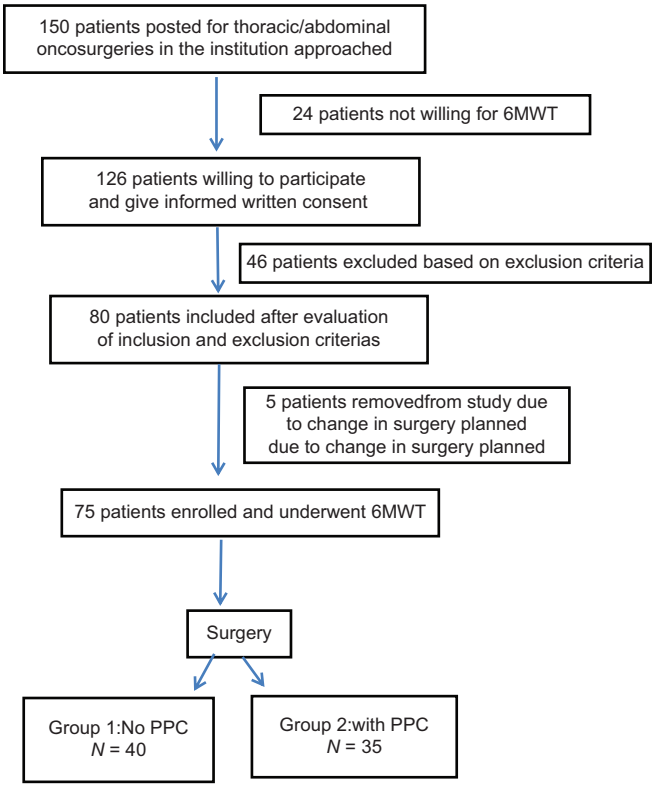

Figure 1: Schematic Representation of Selection of Study Population

Pre-test SpO_2 was significantly lower (P = 0.001) and diastolic blood pressure (77.66 ± 8.228 Vs 72.73 ± 7.362, P = 0.008) was significantly higher in the PPC group [Table 2].

The mean 6MWD of group with PPC was significantly less (344 ± 61.927 m) compared to the group without PPC (442.28 ± 83.194 m) with P value = 0.001 [Table 2].

The duration of hospital stay (17.37 ± 13.49 days Vs 4.88 ± 1.48 days, P = 0.001), intensive care unit (ICU) stay (8.43 ± 8.886, P = 0.001) and mechanical ventilation duration (4.37 ± 9.87, P = 0.001) was also significantly more in those with PPC.

The post-test haemodynamic parameters showed significant variation in systolic BP (140.51 ± 15.252 Vs 130.3 ± 15.875, P = 0.006) and HR (103.74 ± 16.227 Vs 90.53 ± 16.339, P = 0.001) between the two groups [Table 2].

The post 6MWT SpO_2 was significantly lower (94.97 ± 3.451, P = 0.001) and Borg dyspnoea score after test was more in the PPC group (8.69 ± 2.055, P = 0.001).

Combined thoracic and abdominal approach for esophagectomy had higher rates of PPC with 13 out of the 15 patients who underwent this surgery (86.66%) having PPC [Table 3]. Logistic regression analysis of type of surgery (thoracic versus laparotomies versus combined) with PPC showed combined procedures having increased risk compared to thoracic procedures but not significant (P = 0.147, OR = 3.056) with sample size inadequate due to subgrouping. As an associated observation, nine patients were found to have cardiac events in the post-operative period. There were two non-ST elevation MI (NSTEMI) cases, four cases of AF, two SVTs and one VPC with hypotension requiring dual inotropes/vasopressors. The only death in the study group was due to pulmonary thromboembolism and NSTEMI in a patient with severe PPCs requiring prolonged mechanical ventilation. All these patients had 6MWD less than or equal to 390 m. All the patients with cardiac events had post-exercise HR more than or equal to 20% from the pre-test value.

The risk of various haemodynamic parameters and PFT findings for the occurrence of PPC was analysed using logistic regression with median values taken as cut-off in each parameter [Table 4].

Table 2: Comparison of parameters between the PPC groups

Parameters	Group†	*n*	Mean	Std. deviation	*P*
Pre-test SpO_2 (%)	1	40	98.05	1.28	0.001*
	2	35	96.71	1.792	
6MWD (m)	1	40	442.28	83.194	0.001*
	2	35	344	61.927	
Pre-test SBP (mm of Hg)	1	40	128.38	16.428	0.042*
	2	35	135.94	15.035	
Pre-test DBP (mm of Hg)	1	40	72.73	7.362	0.008*
	2	35	77.66	8.228	
Post-test SBP (mm of Hg)	1	40	130.3	15.875	0.006*
	2	35	140.51	15.252	
Post-test DBP (mm of Hg)	1	40	75.9	17.778	0.361
	2	35	78.94	8.711	
Post-test HR (beats per min)	1	40	90.53	16.339	0.001*
	2	35	103.74	16.227	
Post-test SpO_2 (%)	1	40	97.63	1.213	0.001*
	2	35	94.97	3.451	
BORG dyspnoea score post-test	1	40	6.68	1.845	0.001*
	2	35	8.69	2.055	

*P<0.05, †Group 1=without PPC, Group 2=with PPC. HR – Heart rate; SBP – Systolic BP; DBP=diastolic BP

Table 3: Type of surgeries and PPC

Surgery	No. of patients	No. of patients with PPCs *n* (%)
Combined thoracic + abdominal:Esophagectomy	15	13 (86.66)
Abdominal: Colorectal surgery	16	5 (31.25)
Gastrectomy	13	2 (15.31)
Whipples procedure	3	2 (66.66)
Peritonectomy + HIPEC*	3	2 (66.66)
Gynaec-urology surgeries	4	2 (50)
Lung/thoracic surgeries: lobectomy	15	7 (46.66)
VATS†/thoracoscopic surgeries	6	2 (33.33)

*HIPEC – Hyperthermicintraperitoneal chemotherapy. †VATS – Video-assisted thoracoscopic surgery

A 6MWD of below 390 m was significantly associated with PPC, with 76.3% of the patients with PPC having a 6MWD below 390 m (P = 0.001). In the patients with 6MWD more than 390 m, 83.8% were free of PPC. Shorter 6MWD also correlated with longer hospital stay [Table 5].

DISCUSSION

Oncology patients are at very high risk for PPC than general surgical population owing to systemic effects of malignancy, chemotherapy and radiotherapy, impaired nutrition as well as multiple co-morbidities.[3] The PPC rate of our study population was 46.66%, which is slightly higher than the general incidence of PPCs (2–40%).[5] This higher rate is consistent with studies in oncology patients, like by Ozdilekcan *et al*.[3]

Table 4: Association of haemodynamic parameters/risk factors and PPC

Risk factors for PPCs: Univariate analysis	*P*	OR	95% C.I. for OR	
			Lower	Upper
Post-test SBP (>140 vs <=140)	0.063	2.526	0.951	6.711
Post-test DBP (>80 vs upto 80)	0.158	2.267	0.728	7.061
Post-test HR (>98 vs upto 98)	0.020*	3.131	1.197	8.186
Post-test SpO2 (>95 vs Upto 95)	0.002*	0.034	0.004	0.278
Pre-test SBP (>132 vs ≤132)	0.030*	2.821	1.104	7.206
Pre-test DBP (>78 vs ≤78)	0.030*	2.821	1.104	7.206
Pre-test HR (>86 vs upto 86)	0.009*	3.56	1.372	9.237
Pre-test SpO2 (>95 vs Upto 95)	0.059	0.124	0.014	1.086
6MWD (>390 vs<=390)	0.001*	0.060	0.019	0.190
Smoking History (>20 vs ≤20)	0.063	2.526	0.951	6.711
BMI (> 30 vs Upto 18)	0.748	0.6	0.027	13.582
BMI (18-30 vs Upto 18)	0.748	0.6	0.027	13.582
Multivariate analysis of significant factors				
6MWD (>390 vs ≤390)	0.001*	0.028	0.006	0.138
Pre-test Diast BP (>78 vs ≤78)	0.008*	8.597	1.772	41.715
Constant	0.302	1.576		

*P<0.05, SBP – Systolic BP; DBP – Diastolic BP; BMI – Body mass index; vs – Versus

Table 5: 6MWD and length of hospital stay and ICU stay

Factor	6MWD	*n*	Mean Rank	Mann-Whitney U	*P*
Duration of hospital stay	Upto 390 m	38	49.66	260	0.001*
	>390 m	37	26.03		
ICU stay	Upto 390 m	38	50.89	213	0.001*
	>390 m	37	24.76		

*P<0.05, ICU – Intensive care unit

In our study population, all the patients had varying degrees of patient and procedure-related risk factors for PPC, with five patients of ECOG status two. But among them, the findings of functional status assessments by 6MWT varied and significantly correlated with PPC, stressing the necessity of functional exercise testing in pre-operative evaluation.[4,10,11] Even in normal healthy population, functional capacity differs.[12,13] In healthy elderly patients 50 years to 85 years old, 6MWD showed great variability from 383 m to 820 m in the existing literature.[14,15]

Patients understood the test procedure quickly, co-operated with the conduct of the test and all the patients enrolled for the study were able to complete the test without any major complications indicating the safety and ease of this method. Entire process took only an average of 8 min, not costing valuable time as well.

In our study, we found no significant difference in age (62.23 ± 8.423 Vs 59 ± 10.45, P = 0.147) and smoking (42.24 ± 12.862 Vs 34.86 ± 13.98, P = 0.137) in the PPC group, unlike the findings by Keeratichananont *et al*. in Thai patients who found higher age and smoking in PPC group.[5] There was no relation for BMI and serum albumin for PPC unlike existing studies.[16-18] But serum albumin was found to influence 6MWD, indicating nutritional status as a determinant of functional capacity.

Although majority of smokers had more than 20 pack-years history, as part of our pre-operative protocols, we take up patients after quitting smoking for about 2–4 weeks in elective cases. We also observed that the diagnosis of malignancy strongly prompts to quit smoking in most of the patients. This often gives a period of smoking abstinence before surgery. The reformed smoking status is found to reduce pulmonary risks as per Mills *et al*. and our findings may be consistent with this.[19] This further implies smoking as an "independent modifiable risk factor."[3,4,20]

Most of the available literature shows significant correlation of 6MWD with PPC. A 6MWD of below 300 m is at high risk for complications in various patient groups.[21] Ambrosino *et al*. describes this cut-off value as an indicator of early mortality in patients waiting for lung transplant. In our study, we got a cut-off value of 390 m.

On correlating spirometry findings with 6MWD, FEV1 and forced vital capacity (FVC) of below 70% of predicted was found to be associated with lower 6MWD. The FVC ≤70% of predicted was consistently found significant in PPC group and associated with lower 6MWD but FEV1, which is part of many severity indicators of lung diseases like COPD, was not significantly lower in PPC group. A few patients had inadequate PFT performance, but no PPC. Spirometry findings are not consistently associated with risk for PPC. Hence, alternate or adjuvant methods of functional assessment are needed.

A 6MWD of below 400 m is often associated with increased length of hospital stay and high definition unit stay.[21,22] Our findings are also consistent with this, with a cut-off 390 m. Hence, 6MWD is a good indicator of perioperative outcome in line with the existing literature.[23] But no correlation of 6MWD and PPC was shown by Paisani *et al*.[24]

Pneumonia was the most common post-operative pulmonary complication followed by atelectasis and bronchospasm. This was similar to studies by Ozdilekcan *et al*. and Jing *et al*.[3,25] Miskovic and Lumb in their review found respiratory failure as the most frequently observed complication.[9] The evaluation

of haemodynamic parameters increases the scope of 6MWT beyond pulmonary complications. Our analysis showed significant association but relevance can be improved by increasing sample size. Often oxygen saturation by pulse oximetry ≤89% or a 4% fall below baseline value post-exercise is described as significant risk for PPC.[26] But we found even 2–3% fall from baseline and SpO_2 <95% had significance. Post-exercise increase in heart rate, blood pressure and Borg dyspnoea scores were significantly associated with complications and lesser 6MWD. This indicates limitation in exercise tolerance even at submaximal level.

Comparison between other exercise tests was not done in our study, which is a limitation. Solway *et al*. in their study showed that a 6MWD of more than 1,000 feet and a stair climb of greater than 44 steps as predictive of successful surgical outcome.[27] Significant correlation between mean 6MWD (310 ± 100 m) and peak oxygen uptake by CPET (12.2 ± 4.5 ml/kg/min, *P* value < 0.001) was found by Cahalin *et al*.[27,28] Incremental shuttle walk test (ISWT) was found to be superior in this 2016 study.[27] In addition, in order to meet all requirements, we conducted the test in a track 25 m long which is lesser than the recommended distance of 30 m but allowed. Shorter track may cause variations in 6MWD.[1,12] Further improvements are possible in our study by comparing with other exercise tests and data from healthy population of same ethnicity, including correlations for anthropometry of patients, preventive measures implemented, intraoperative haemodynamics, transfusion details, biochemical parameters as well as evaluation of complications for a longer duration and larger sample size.

CONCLUSION

Six-minute walk test is a reliable, inexpensive predictor of post-operative pulmonary complications with a cut-off 6MWD of 390 m in oncosurgery patients. The scope for research in the utility and significance of 6MWT is enormous and should be explored.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity.

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Conflicts of interest

There are no conflicts of interest.

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Cut Off Date	Name of Award / Competition	Application to be sent to
30 June 2020	Bhopal Award for Academic Excellence	Hon. Secretary, ISA (by log in & E Mail)
30 June 2020	Late Prof. Dr. A .P. Singhal Life Time Achievement Award	Hon. Secretary, ISA (by log in & E Mail)
30 June 2020	Rukmini Pandit Award	Hon. Secretary, ISA (by log in & E Mail)
30 June 2020	Dr. Y. G. Bhoj Raj Award	Hon. Secretary, ISA (by log in & E Mail)
30 June 2020	Mrs. Shashi & Dr. P Chandra Award	Hon. Secretary, ISA (by log in & E Mail)
30 Sept 2020	Kop's Award	Chairperson, Scientific Committee ISACON 2020 copy to Hon. Secretary, ISA (by log in & E Mail)
30 Sept 2020	ISACON Jaipur Award	Chairperson, Scientific Committee ISACON 2020 copy to Hon. Secretary, ISA (by log in & E Mail)
30 Sept 2020	Prof. Dr. Venkata Rao Oration 2020	Hon. Secretary, ISA (by log in & E Mail)
30 Sept 2020	Ish Narani Best poster Award	Chairperson, Scientific Committee ISACON 2020
30 Sept 2020	ISA Goldcon Quiz	Chairperson, Scientific Committee ISACON 2020
10 Nov 2020	Late Dr. T. N. Jha Memorial Award & Dr. K. P. Chansoriya Travel Grant	Hon. Secretary, ISA, (by log in & E Mail) copy to Chairperson Scientific Committee ISACON 2020
20 Oct 2020	Bidding Application for ISACON 2022	Hon.Secretary, ISA by log in, E Mail & hard copy
20 Oct 2020	Awards (01 Oct 2018 to 30 Sept 2020)	Hon. Secretary, ISA (by log in & E Mail)

(Report your monthly activity online every month after logging in using Branch Secretary's log in ID)

1. Best City Branch
2. Best Metro Branch
3. Best State Chapter
4. Public Awareness – Individual
5. Public Awareness – City / Metro
6. Public Awareness - State
7. Ether Day (WAD) 2020 City & State
8. Membership drive
9. Proficiency Awards

Send hard copy (only for ISACON 2022 bidding) to

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