

Original Article

The hemorrhage risk of patients undergoing bronchoscopic examinations or treatments

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Abstract: Background: In recent years, bronchoscopic procedures have become more complex and sophisticated, as well as more extensively used. This study aimed to evaluate the safety, particularly the hemorrhage risk, of patients undergoing bronchoscopic examinations or treatments. Methods: This retrospective study consisted of inpatients and outpatients who underwent bronchoscopic examinations or treatments in our respiratory department between January 1, 2008 and December 31, 2019. We collected and analyzed the patient and bronchoscopic data. Results: Among the 45,734 patients who underwent diagnostic or therapeutic bronchoscopies, the severe complication rate was 0.85%, and the mortality was 0.01%. The severe complication rates varied significantly among the types of bronchoscopic procedures; the rate was higher with therapeutic bronchoscopies than with exploratory examination or biopsy bronchoscopies. Bleeding was the most common severe complication, and it occurred more frequently with biopsies in the left upper lobe and the bronchus intermedius, but its incidence decreased as the number of biopsies increased above one. Conclusions: Although bronchoscopic procedures have become more complex and sophisticated, bronchoscopies are still well tolerated. However, precautions should be taken because hemorrhaging and pneumothorax remain potential complications, and they can be fatal.

Keywords: Hemorrhage, bronchoscope, complications

Introduction

With advances in bronchial intervention technology in recent years, bronchoscopic examinations and treatments have become extensively used by respiratory physicians and pulmonologists for both diagnostic and therapeutic purposes [1]. Hence, the current safety of bronchoscopy is an important issue that warrants consideration.

Almost all previous studies [2-4] concluded that bronchoscopy is generally well tolerated, with complications occurring in less than approximately 6% of procedures and mortality in less than 0.1% [3, 5, 6]. The most frequent complications are hemorrhaging, oxyhemoglobin desaturation, pneumothorax, and pulmonary edema. Bleeding is the most common complication, with an incidence varying between 0.5 to 5.3%, depending on the endoscopic proce-

dures and the underlying disease [7-10]. To reduce the direct morbidity and mortality associated with the complications, bronchoscopy centers should design emergency response plans that include the immediate availability of rescue drugs and equipment. Experienced bronchoscopists and thoracic surgeons are also essential.

Most bleeding that occurs during a bronchoscopy is controllable, but massive hemorrhaging can be life-threatening. Massive hemorrhaging can obstruct the airway within a short time, and the use of the lateral decubitus position provides a basic rescue maneuver to allow time for subsequent treatment. Tracheal intubation may be necessary to maintain a patient's airway, and topical and intravenous hemostatic agents, urgent bronchial artery embolization, and emergency surgery are treatment options. In a previous study, the average fatality rate in patients

The hemorrhage risks of patients undergoing bronchoscopy

with massive bleeding was found to be 10.8%, with older age (≥ 65 years), localized tracheal bleeding, higher blood loss (≥ 500 mL), and the occurrence of shock being associated with a higher risk of death [7].

As hemorrhaging is one of the most difficult management problems for the bronchoscopist, identifying the risk factors for bronchoscopy-induced bleeding is necessary to enhance patients' safety. However, the clinical factors predictive of hemorrhage have been rarely reported. In addition, bronchoscopy has undergone many advances over the years, expanding its overall use and leading to the development of more complex and sophisticated procedures. Therefore, the aim of this study was to evaluate the safety, and especially the hemorrhage risk, of outpatients and inpatients undergoing bronchoscopic examinations or treatments.

Methods

This retrospective study was conducted to evaluate the safety (particularly the hemorrhage risk) of patients undergoing bronchoscopies for diagnosis or treatment. Both outpatients and inpatients were included. The regional ethics committee of our institution (Tangdu Hospital) approved this study (approval no. TDLL2013027). The committee waived the requirement for patient consent because of the retrospective nature of this study. We collected data regarding all the patients who underwent bronchoscopic examinations or treatments at our respiratory department between January 1, 2008 and December 31, 2019. A total of 45,734 patients were included in this study.

To exclude the patients for whom bronchoscopy was contraindicated, routine blood tests, blood coagulation assessments, and electrocardiograms were obtained before the procedure. The patients were also instructed to discontinue anticoagulant or antiplatelet medications 72 hours before the bronchoscopy and to abstain from food and water for 6 hours before the procedure.

General information, such as sex, age, and hospitalization status (outpatient or inpatient), was collected for each patient. The bronchoscopy information was also recorded and analyzed, including the type of procedure, the bronchoscope's external diameter, the type of anesthe-

sia, the biopsy method, the biopsy site, the number of biopsies, the therapeutic method, the complications, and the severity of the bleeding. The type of anesthesia was local or general anesthesia; local anesthesia was achieved with topical tetracaine. The bronchoscopic procedures were divided into exploratory examinations, biopsy bronchoscopies, and therapeutic bronchoscopies. An exploratory examination was defined as a simple bronchoscopic evaluation, with no biopsy or therapy. Biopsy bronchoscopies included bronchial biopsies, transbronchial needle aspiration biopsies, bronchoalveolar lavages, and brush biopsies. Therapeutic bronchoscopy was defined as a therapeutic operation performed using bronchoscopy, including laser irradiation, argon plasma, freeze thawing, freeze cutting, foreign body forceps or baskets, balloon dilatation, electric snare ligation, rigid bronchoscopic circumscision, and stent positioning.

The following severe complications were recorded: severe hypoxemia requiring increased ventilator support during the procedure or the termination of the procedure, pneumothorax, severe arrhythmias requiring intervention or a premature termination of the procedure, cardiac arrest, unplanned hospital admission or intensive care unit (ICU) transfer, severe bleeding requiring intervention (grades 3 and 4, as defined below), death, and other severe complications. The distribution of the complications associated with each type of procedure was determined. There are no standard criteria for evaluating the severity of bleeding during bronchoscopy, as airway secretions mix with blood, leading to difficulties with quantifying the amount of bleeding. Therefore, we classified the bleeding severity into 5 grades [11, 12]. Grade 0: no bleeding or extremely minimal bleeding that did not require suctioning, grade 1: mild bleeding that required only suctioning, grade 2: bleeding that required the topical instillation of epinephrine or ice-cold saline, grade 3: bleeding that required pressure via an inflated balloon catheter or intravenous pituitrin (a pituitary extract containing vasopressin), and grade 4: bleeding that required hemodynamic support, the transfusion of blood products, or interventional or surgical therapy. The severity of the bleeding associated with each type of bronchoscopy, the site of the biopsy, and the number of biopsies were analyzed. The

The hemorrhage risks of patients undergoing bronchoscopy

Table 1. Characteristics of the study population

Items	Inpatients (n = 27215)	Outpatients (n = 18519)	Total (n = 45734)	Analytic result	P value
Male	18082 (66.44%)	9180 (49.57%)	27262	$\chi^2 = 1303$, df = 1	< 0.01
Female	9133 (33.56%)	9339 (50.43%)	18472		
Age (year)	55.3 ± 15.25	44.34 ± 18.47		t = 63.7	< 0.05
Anesthesia type					
Local anesthesia	26224	18108	44332		
General anesthesia	991	411	1402		
Number of Complications					
Hypoxemia requiring termination of procedure	42	15	57		0.03
Bleeding and hemoptysis	173	64	237		< 0.01
Pneumothorax	36	4	40		< 0.01
Cardiac arrhythmias or cardiac arrest	25	7	32		0.03
Unplanned hospital admission or ICU transfer	12	2	14		0.06
Death	2	2	4		> 0.99
Others	4	0	4		0.15
Total	294	94	388		< 0.01
Bronchoscope type					
Explorative examinations	5667 (20.82%)	5539 (29.91%)	11206		
Biopsies	18056 (66.35%)	8839 (47.73%)	26895		
Therapeutic bronchoscopies	3492 (12.83%)	4141 (22.36%)	7633		

The data are presented as n/N (%) or as the mean ± standard deviation (n) (range).

distribution of the complications according to bronchoscope external diameter was also evaluated.

The data were reported as the mean ± standard error. To compare the groups, unpaired *t* tests were used for the continuous data, and Fisher's exact tests were used for the count data. Differences in mean values were considered significant at *P* < 0.05.

Results

Patient characteristics

The characteristics of the study population are presented in **Table 1**. Among the 45,734 patients included in this study, 27,215 were inpatients, and 18,519 were outpatients, with mean ages of 55.3 and 44.3 years, respectively. The inpatients were significantly older than the outpatients (*P* < 0.05). There were 27,262 males and 18,472 females. In total, 11,206 patients underwent exploratory examinations, 26,895 patients underwent biopsy bronchoscopies, and 7,633 patients underwent therapeutic bronchoscopies. Most of the procedures were performed using local anesthesia, but 3.1% (1,402/45,734) were performed under

general anesthesia. The overall incidence of severe complications was significantly higher in the inpatients than in the outpatients (*P* < 0.01). Several individual complications were also more frequent in inpatients, including severe bleeding and hemoptysis (*P* < 0.01), pneumothorax (*P* < 0.01), severe hypoxemia (*P* = 0.03), and cardiac arrhythmias (*P* = 0.03).

Distribution of the severe complications

We identified 388 severe complications, including 57 cases of severe hypoxemia, 40 cases of pneumothorax, 32 cases of severe arrhythmias and cardiac arrest, 14 cases of unplanned hospital admission or ICU transfer, 237 cases of severe hemorrhaging (grades 3 and 4 bleeding), 4 deaths, and 4 cases of other severe complications (**Tables 2, 3** and **S1**). Therefore, the incidence of severe complications was 0.85%, and the mortality rate was 0.01%. The complication rates of the different types of bronchoscopic procedures varied significantly ($\chi^2 = 14.43$, df = 2, *P* < 0.01), with the complication rate being higher with therapeutic bronchoscopies (1.21%) than with exploratory examinations (0.72%) or biopsy bronchoscopies (0.80%). The most common complication was severe bleeding, particularly during bron-

The hemorrhage risks of patients undergoing bronchoscopy

Table 2. Complications and severity of the bleeding associated with the various types of procedures

Type of procedure	No. of complications	Tot cases	% out of Tot cases	No. of Bleeding cases	Tot cases	% out of Tot cases
Explorative examinations	81	11206	0.72	649	11206	5.79154
Biopsies	215	26895	0.80	11126	26895	41.36828
Therapeutic bronchoscopies	92	7633	1.21	2882	7633	37.75711
Analysis	$\chi^2 = 14.43$, $df = 2$, $P < 0.01$; Explorative examinations vs. Therapeutic bronchoscopies $P < 0.05$; Biopsies vs. Therapeutic bronchoscopies $P < 0.05$			$\chi^2 = 4735$, $df = 2$, $P < 0.01$; Explorative examinations vs. Biopsies $P < 0.05$; Therapeutic bronchoscopies $P < 0.05$		

The data are presented as n/N (%) or as the mean \pm standard deviation (n) (range).

Table 3. General table of complications recorded

Complications	No.	% of total complications	% of total procedures
Hypoxemia requiring termination of procedure	57	14.69	0.12
Bleeding and hemoptysis	237	61.08	0.52
Pneumothorax	40	10.31	0.09
Cardiac arrhythmias or cardiac arrest	32	8.25	0.07
Unplanned hospital admission or ICU transfer	14	3.61	0.03
Death	4	1.03	0.01
Others	4	1.03	0.01

The data are presented as n/N (%) or as the mean \pm standard deviation (n) (range).

chial biopsies. During the exploratory examinations, the most common complication was hypoxemia, with an incidence of 0.25%.

Severity of the bleeding during the bronchoscopies

Because bleeding is potentially fatal and because it is the most common complication during bronchoscopies, we examined this complication in detail. We first analyzed the severity of the bleeding associated with the type of bronchoscopic procedure (**Tables 2** and **S2**). The overall incidence of hemorrhaging (any severity) was significantly higher with biopsy bronchoscopies (41.37%) than with exploratory examinations (5.79%) or therapeutic bronchoscopies (37.76%) ($\chi^2 = 4735$, $df = 2$, $P < 0.01$). Nearly half (41.37%) of all patients who underwent biopsies, particularly bronchial biopsies, developed varying amounts of bleeding; the bleeding was usually mild (grades 1 or 2), but 1.47% of the patients experienced severe bleeding. For therapeutic bronchoscopies, the overall incidence of hemorrhaging (any severity) was 37.76%, and the incidence of severe bleeding was 1.63%.

Severity of the bleeding associated with the biopsy site and the number of biopsies

The severity of the bleeding associated with the biopsy site and the number of biopsies was also explored. The overall incidence of hemorrhaging (any severity) was higher in the left upper lobe (62.50%) and in the bronchus intermedius (62.79%) than at other locations (**Tables 4** and **S3**). The severe bleeding rate was also higher in the bronchus intermedius (2.07%). The overall bleeding rate (84.08%) and the severe bleeding rate (4.33%) were both higher when the number of biopsies was one, compared with more than one (**Tables 5** and **S3**). The overall bleeding rate decreased as the number of biopsies increased above 1 ($\chi^2 = 51.61$, $df = 1$, $P < 0.01$).

The distribution of the severe complications according to bronchoscope external diameter

The overall incidence of severe complications differed according to the external diameter of the bronchoscope ($\chi^2 = 21.33$, $df = 5$, $P < 0.01$). However, there was no significant association between bronchoscope external diameter and

The hemorrhage risks of patients undergoing bronchoscopy

Table 4. Severity of the bleeding associated with the biopsy site

Type of procedure	No. of Bleeding cases	Tot cases	% out of Tot cases	G3 + G4	% out of Tot cases
Biopsy site					
Right upper lobe	2616	4447	58.83	33	0.74
Right middle lobe	1009	1775	56.85	15	0.85
Right lower lobe	1509	2821	53.49	15	0.53
Left upper lobe	2858	4573	62.50	48	1.05
Left lower lobe	1957	3447	56.77	26	0.75
Trachea	116	285	40.70	0	0
Right main bronchus	130	226	57.52	1	0.44
Left main bronchus	230	411	55.96	5	1.22
Bronchus intermedius	243	387	62.79	8	2.07
Lingula	269	487	55.24	3	0.62
Unclear	11	158	6.96	0	0
Analysis	$\chi^2 = 106.7$, df = 9, P < 0.01			$\chi^2 = 17.64$, df = 9, P = 0.04	

The data are presented as n/N (%) or as the mean \pm standard deviation (n) (range).

Table 5. Severity of the bleeding associated with the number of biopsies

Type of procedure	No. of Bleeding cases	Tot cases	% out of Tot cases	G3 + G4	% out of Tot cases
Biopsies number					
	17938				
1	486	578	84.08	25	4.33
2	587	822	71.41	19	2.31
3	900	1516	59.37	15	0.99
4	1062	2431	43.69	10	0.41
5	6569	11071	59.34	66	0.60
6	594	988	60.12	7	0.71
7	62	125	49.60	0	0.00
> 7	238	407	58.48	3	0.74
Analysis	$\chi^2 = 51.61$, df = 1, P < 0.01			$\chi^2 = 64.62$, df = 1, P < 0.01	

The data are presented as n/N (%) or as the mean \pm standard deviation (n) (range).

the distribution of complications ($\chi^2 = 7.473 \times 10^{-5}$, df = 1, P = 0.09931) (**Table 6**).

Discussion

In recent decades, bronchoscopy has undergone considerable developments and extensive use, and the types of bronchoscopic procedures have evolved, becoming more complex and sophisticated [1]. Because of the noncontemporaneous nature of previous studies, it is necessary to reanalyze the incidence and types of complications associated with bronchoscopy. Therefore, we conducted this study to evaluate the safety, particularly the hemorrhage risk, of both outpatients and inpatients undergoing bronchoscopic examinations or treatments.

A few studies have reported the complications and mortality rates associated with bronchos-

copy [2, 13-16]. In a study of 20,986 bronchoscopies [3], the most common complications were hemorrhaging, oxyhemoglobin desaturation, pneumothorax, and pulmonary edema, with an overall complication rate of 1.08% and a mortality rate of 0.02%. According to a postal survey conducted by Simpson et al. [6], the major complication and mortality rates with bronchoscopies were 0.12% and 0.04%, respectively. Smyth and Stead [17] pointed out a similar mortality rate (0.045%) in their survey-based study. However, other studies have revealed overall complication rates of approximately 5% [18]. For some types of procedures, such as cryobiopsy, the incidence of hemorrhaging alone reached 42.1% [11, 19]. Although the authors of most previous studies concluded that bronchoscopy is well tolerated, the rates of the specific complications associated with the different operations have not been

The hemorrhage risks of patients undergoing bronchoscopy

Table 6. The distribution of the complications by bronchoscope diameter

Complications	No.	3.6 mm	4.0 mm	4.9 mm	5.6 mm	5.9 mm	6.9 mm	Unknown
Hypoxemia requiring termination of procedure	57	2/2133	0/2429	39/27262	2/2558	12/9679	0/366	2/1307
Bleeding and hemoptysis	237	2/2133	17/2429	159/27262	3/2558	40/9679	1/366	15/1307
Pneumothorax	40	1/2133	0/2429	24/27262	1/2558	12/9679	0/366	2/1307
Cardiac arrhythmias or cardiac arrest	32	2/2133	1/2429	20/27262	0/2558	8/9679	0/366	1/1307
Unplanned hospital admission or ICU transfer	14	0/2133	1/2429	8/27262	1/2558	4/9679	0/366	0/1307
Death	4	0/2133	0/2429	2/27262	0/2558	2/9679	0/366	0/1307
Others	4	0/2133	0/2429	3/27262	0/2558	1/9679	0/366	0/1307
Total	388	7/2133	19/2429	255/27262	7/2558	79/9679	1/366	20/1307
Analysis		$\chi^2 = 21.33$, $df = 5$, $P < 0.01$; Trend: $\chi^2 = 7.473e-005$, $df = 1$, $P = 0.09931$						

The data are presented as n/N (%) or as the mean \pm standard deviation (n) (range).

evaluated in detail. In addition, the risk factors for bronchoscopy-related hemorrhaging have rarely been comprehensively analyzed.

In this study, the severe complication and mortality rates with bronchoscopies were 0.85% and 0.01%, respectively, which are consistent with the rates reported previously. The most frequent severe complication was bleeding. Bleeding of any severity occurred in approximately one-third of the patients, but it was usually mild and easily controlled. Importantly, the overall bleeding rate was higher when the biopsies were obtained from the left upper lobe and bronchus intermedius, and the severe bleeding rate was highest for the biopsies of the bronchus intermedius. These findings may be attributed to the bronchus intermedius being located adjacent to the blood vessels.

The overall bleeding rate (84.08%) and the severe bleeding rate (4.33%) were both higher when only one biopsy was performed, compared with more than one. Moreover, the proportion of bleeding cases decreased as the number of biopsies increased. This inverse relationship between the bleeding rate and the number of biopsies may reflect the bronchoscopists ceasing to obtain further biopsies when bleeding occurred, although ≤ 4 block specimens might be insufficient for diagnosis.

Another finding that requires mentioning was the higher severe complication rate in inpatients (1.08%) than in outpatients (0.51%). This may have been because the inpatients were significantly older, increasing the likelihood of comorbidities.

Our study had some limitations. First, this retrospective study had the usual risk of bias inherent in this study design. Second, there were

relatively low numbers of patients undergoing some types of therapeutic bronchoscopy (e.g., transbronchial needle aspiration biopsies, laser treatments, freeze cuttings, and rigid bronchoscopic circumscisions), limiting our ability to provide comprehensive safety information for all the possible procedures. Third, owing to the difficulties of collecting patient data, such as the prothrombin times and the activated partial thromboplastin time results, we could not comprehensively analyze the risk factors for hemorrhage.

Conclusions

Although bronchoscopic procedures have become more complex and sophisticated in recent years, bronchoscopy remains a generally safe and well-tolerated procedure. However, the severe complications and mortality have not decreased over the years. Precautions continue to be required because of the risks of severe complications, such as hemorrhaging and pneumothorax, are still present, and these complications can be fatal.

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Disclosure of conflict of interest

None.

Abbreviations

ICU, intensive care unit.

The hemorrhage risks of patients undergoing bronchoscopy

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The hemorrhage risks of patients undergoing bronchoscopy

Table S1. Distribution of the complications associated with the procedure types

Type of procedure	Hypoxemia requiring termination of procedure	Bleeding and hemoptysis	Pneumothorax	Cardiac arrhythmias or cardiac arrest	Unplanned hospital admission or ICU transfer	Death	Others	No. of complications	Tot cases	% out of Tot cases
Explorative examinations	28	26	3	17	4	1	2	81	11206	0.72
Biopsies	15	164	24	8	3	1	0	215	26895	0.80
Bronchial biopsy	4	150	10	7	2	1	0	174	18661	0.93
Transbronchial needle aspiration biopsy	0	0	1	0	0	0	0	1	389	0.26
Bronchoalveolar lavage	10	59	17	1	0	0	0	87	14847	0.58
Brush biopsy	0	6	0	2	0	0	0	8	776	1.03
Others	1	2	0	0	1	0	0	4	13	30.77
Therapeutic bronchoscopies	14	47	13	7	7	2	2	92	7633	1.21
Laser	0	5	0	0	0	0	0	5	52	9.62
Argon plasma	3	25	1	1	2	0	1	33	2409	1.37
Freeze thawing	8	32	3	5	5	2	1	56	4755	1.18
Freeze cutting	0	3	0	0	1	1	0	5	61	8.20
Foreign body forceps or basket	0	2	3	0	0	0	0	5	442	1.13
Balloon dilatation	4	2	5	1	1	1	0	14	1241	1.13
Electric snare ligating	2	18	0	2	3	0	0	25	429	5.83
Rigid bronchoscopic circumcission	1	4	0	1	1	0	0	7	78	8.97
Stent position	1	1	0	0	0	0	0	2	163	1.23
Others	1	3	2	1	1	0	1	9	123	7.32

The data are presented as n/N (%) or as the mean \pm standard deviation (n) (range).

The hemorrhage risks of patients undergoing bronchoscopy

Table S2. The severity of the bleeding associated with the procedure type

Type of procedure	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	No. of Bleeding cases	Tot cases	% out of Tot cases
Explorative examinations	10557	552	71	21	5	649	11206	5.79154
Biopsies	15769	10009	953	160	4	11126	26895	41.36828
Bronchial biopsy	7915	9669	933	147	3	10752	18667	57.59897
Transbronchial needle aspiration biopsy	347	41	1	0	0	42	389	10.79692
Bronchoalveolar lavage	10455	4094	239	59	0	4392	14847	29.58173
Brush biopsy	389	323	58	6	0	387	776	49.87113
Others	8	2	3	1	1	7	15	46.66667
Therapeutic bronchoscopies	4751	2677	158	42	5	2882	7633	37.75711
Laser	34	11	2	5	0	18	52	34.61538
Argon plasma	1452	874	58	23	2	957	2409	39.72603
Freeze thawing	2743	1875	105	28	4	2012	4755	42.31335
Freeze cutting	34	24	0	2	1	27	61	44.2623
Foreign body forceps or basket	318	114	8	2	0	124	442	28.0543
Balloon dilatation	855	362	22	1	1	386	1241	31.10395
Electric snare ligating	228	163	20	15	3	201	429	46.85315
Rigid bronchoscopic circumcission	63	10	1	4	0	15	78	19.23077
Stent position	142	19	1	1	0	21	163	12.88344
Others	98	20	2	3	0	25	123	20.3252

The data are presented as n/N (%) or as the mean ± standard deviation (n) (range).

The hemorrhage risks of patients undergoing bronchoscopy

Table S3. The severity of the bleeding associated with the biopsy site and the number of biopsies

Type of procedure	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	No. of Bleeding cases	Tot cases	% out of Tot cases
Biopsy site								
Right upper lobe	1831	2368	215	32	1	2616	4447	58.82617
Right middle lobe	766	905	89	15	0	1009	1775	56.84507
Right lower lobe	1321	1382	112	14	1	1509	2821	53.49167
Left upper lobe	1715	2550	260	48	0	2858	4573	62.49727
Left lower lobe	1490	1754	177	26	0	1957	3447	56.77401
Trachea	169	107	9	0	0	116	285	40.70175
Right main bronchus	96	111	18	1	0	130	226	57.52212
Left main bronchus	181	192	33	5	0	230	411	55.96107
Bronchus intermedius	144	209	26	7	1	243	387	62.7907
Lingula	218	247	19	3	0	269	487	55.23614
Unclear	147	11	0	0	0	11	158	6.962025
Biopsies number	17938							
1	98	352	109	25	0	486	578	84.08304
2	235	480	88	18	1	587	822	71.41119
3	616	776	109	14	1	900	1516	59.36675
4	1369	905	147	10	0	1062	2431	43.68573
5	4502	6141	362	65	1	6569	11071	59.3352
6	394	531	56	7	0	594	988	60.12146
7	63	59	3	0	0	62	125	49.6
> 7	169	211	24	3	0	238	407	58.47666

The data are presented as n/N (%) or as the mean \pm standard deviation (n) (range).