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Laryngectomees' views on laryngeal transplantation

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Abstract Loss of a functional larynx has marked implications for quality of life that remain after both laryngectomy and its alternatives. One solution is laryngeal transplantation. We hypothesised that laryngeal transplantation would be unacceptable to a population of laryngectomees, and that such a lack of acceptability would not be affected by age, sex or time elapsed since operation. In addition, we sought the views of laryngectomees on priorities for research. A questionnaire was developed and mailed to 1000 members of laryngectomee clubs. A total of 372 of 404 responses were suitable for analysis. Seventy-five percent of the respondents said they would accept a transplant under ideal conditions; the number dropped to 58.9 % when a stoma was to be retained. Fifty percent would accept a graft even if it did not result in a normal voice. A positive response was more likely in younger respondents ($P < 0.001$ all questions; linear regression). Some 47.3 % of respondents thought research money could be better spent on other projects, and this response was commoner in older respondents ($P = 0.0001$). Highest priorities for research into laryngeal cancer were development of new treatments (63.2 %), prevention (60.2 %) and optimisation of quality of life (57 %). In short, there appears to be a surprisingly high level of support for laryngeal transplantation amongst those who have had a laryngectomy.

Key words Larynx transplantation · Laryngectomy · Questionnaire

Introduction

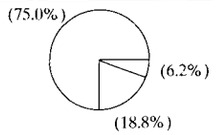
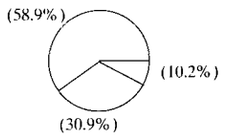
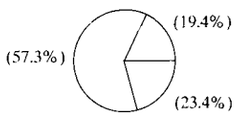
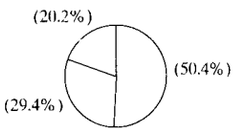
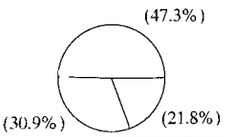
Once the immediate postoperative phase has been successfully negotiated, persons who have had a laryngectomy are often ill-prepared for a lifestyle that may be radically different from previous experience. Preservation of a good airway requires an acceptable tracheostome, with its concurrent problems. Loss of control of the upper airway sphincter leads to obvious difficulties with bathing, swimming and heavy lifting. The decrease in efficacy of the nasal airway results in marked impairment in senses of taste and smell, and dysphagia may further reduce the pleasure of eating. Loss of functioning thyroid tissue may have long-term endocrinological implications. Methods of replacing phonation have met with mixed success [2, 17]. Whilst large series report up to 90 % "excellent" objective voice results following the use of various voice prostheses, this is probably a poor surrogate for the actual disability encountered by laryngectomees at the personal level [16].

Considering this level of morbidity, both patients and surgeons have looked for ways to avoid laryngectomy. Twenty percent of men in one survey said they would prefer radiotherapy to save their larynx, even if their chances of survival were significantly reduced [4]. Increasingly, many surgeons practice laryngeal conservation surgery, despite the consequent reduction in the oncological safety margin. A possible solution is laryngeal transplantation [1, 7, 13].

Table 1 Characteristics of the study sample (*d. o. b.* date of birth, *SD* = standard deviation)

	Number of respondents	Median d. o. b.	Mean d. o. b.	SD (days)	Median date of laryngectomy	Mean date of laryngectomy	SD (days)
Males	306 (82.3 %)	3/4/27	13/1/29	3750	14/2/92	16/4/90	2059
Females	66 (17.7 %)	19/11/29	13/6/31	3651	1/5/92	7/8/90	2433
Total sample	372	8/1/28	18/1/28	3527	8/3/92	20/5/90	2112

Table 2 Questions regarding laryngeal transplantation and responses (numbers and percentages, displayed as pie-charts)

	Yes	No	Don't know	
Question 1 If it were completely safe and simple to receive a transplanted larynx, would you wish to have the operation?	279	70	23	
Question 2 If it were safe and simple but meant keeping a stoma for breathing, would you want to receive a transplanted larynx?	219	115	38	
Question 3 If it meant a stay of 28 days in hospital, would you want to receive a transplanted larynx?	256	85	31	
Question 4 If it involved significant risk to your life whilst in hospital (e. g. because of the need to stop your immune system from working fully) would you want to receive a transplanted larynx?	72	213	87	
Question 5 If there was no guarantee of a normal voice after transplantation, but everything else was satisfactory would you wish to receive a transplanted larynx?	137	80	55	
Question 6 Do you think we would be better to spend the time and money on another form of research into laryngeal cancer and the people it affects?	176	115	81	

Early animal studies were carried out in the United States using a canine model with varying degrees of success [15, 19, 25], and in 1969 a non-revascularised human transplant took place in Belgium [9]. Despite the unsophisticated immunosuppression, the graft took well before the patient died of locally recurrent carcinoma. The recent success of the first true human laryngeal allograft has led to further optimism [1]. Recently, work with a rat model [23, 24] has been promising, and a porcine model has been usefully employed for tracheal [12] and laryngeal [unpublished work] transplantation. In fact, major advances in surgery, immunology and transplantation science in the last 20 years have made the long-term human laryngeal allograft a possibility [13]. However, before embarking on lengthy and costly research, it is important to determine what potential recipients might think of the concept.

The hypothesis under test in the present paper is that a population of laryngeal carcinoma patients who have already undergone a laryngectomy would not find a laryngeal transplant an acceptable alternative to life without a larynx. The primary aim of this study is to discover

Table 3 Results of linear regression testing for questions (given here in abbreviated form) on transplantation. (*B* partial regression coefficient, *beta* actual beta weight for variables entered into model or "beta if entered" for others, Sig T significance level of T-testing)

Question	Variable	B	Beta	Sig T
1. Completely safe	Age[a]	0.3	0.18	0.0006*
	Sex		0.06	0.3
	Time[a]	0.2	0.13	0.02
2. Retention of stoma	Age[a]	0.21	0.11	0.04
	Sex		−0.02	0.7
	Time[a]	0.21	0.11	0.04
3. Long hospital stay	Age[a]	0.3	0.17	0.001*
	Sex		0.02	0.7
	Time[a]	0.16	0.09	0.09
4. Life-threatening	Age[a]	0.37	0.19	0.0003*
	Sex		−0.4	0.5
	Time		0.03	0.6
5. No definite voice	Age[a]	0.5	0.26	0.0001*
	Sex		−0.02	0.8
	Time		0.17	0.7
6. Prefer other research	Age[a]	−0.42	−0.22	0.0001*
	Sex		0.004	0.9
	Time		0.04	0.5

* $P < 0.01$
[a] Variable included in final model

to what extent the option of laryngeal transplantation would be acceptable to such a population, whilst a secondary aim of this paper is to discover what priorities patients with a laryngectomy put on different forms of research into laryngeal cancer and its treatment.

Patients and methods

A questionnaire was initially drafted by brainstorming with a multidisciplinary group involved in the care of patients with head and neck cancer. The results were presented to a panel consisting of a consultant ENT surgeon, a district nurse and a statistician who drew up a preliminary questionnaire. This was shown to 20 laryngectomy patients attending outpatient clinics in Bristol. This resulted in a clarifying of the introductory statements and a reduction in the number of free-response questions. This revised draft was then sent to ten patients in the study group, randomly selected from the mailing list of the National Association of Laryngectomee Clubs (NALC). After this initial mail-shot, further modifications were made, including questions related to demographics in order to gauge the representativeness of the study group.

A total of 1000 questionnaires with reply-paid envelopes were sent to NALC in December 1995 for distribution with the Association's newsletter to the 96 affiliated laryngectomee clubs. Due to the number of healthcare workers and possibly deceased members amongst the 3000 on the association's mailing list, distribution of questionnaires took place at a local level by individual clubs. Only a single mailing took place. Replies were sent to the otorhinolaryngology department at Bristol University and collected until February 1997.

The final questionnaire consisted of an introductory explanatory statement in lay language, followed by questions related to the age, sex and survival time since laryngectomy of the respondent. Six questions related to the acceptability of a laryngeal transplant under different conditions, followed by six questions about the direction of future research. A final free-response section was also included.

Results are mainly expressed descriptively. A model was proposed whereby the answers to such questions were dependent on the age and sex of the respondent. It was also felt that the response was likely to be affected by the amount of time that had elapsed since laryngectomy. This model was tested by backward, stepwise, linear regression with the answer to the question ("yes", "no", "don't know") as the dependent variable. The level of significance was taken as 1 %. Statistical software used was SPSS (Manchester Computing Centre, version 6.1).

Results

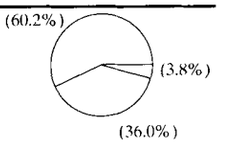
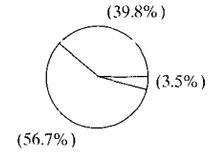
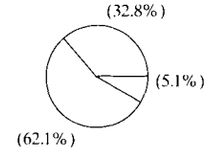
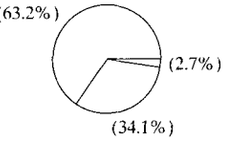
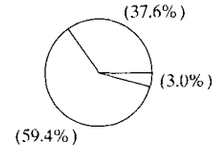
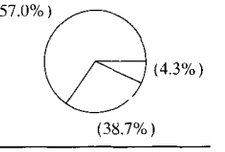
A total of 404 responses were obtained. Thirty-two were unsuitable for inclusion as replies were illegible, incomplete, or the respondent had not actually undergone a laryngectomy.

Table 1 shows the demographic data of the sample. Some 82.3 % of the respondents were male and 17.7 % female, with a mean date of birth in January 1928, giving an approximate age of 67 (SD ± 10 years) at the time of response. The mean operation date was May 1990, giving an approximate average survival time since operation of 6 years (SD ± 6 years).

Table 2 shows the responses to questions relating to the acceptability of laryngeal transplantation. Seventy-five percent of respondents would accept a completely safe transplant under ideal conditions; the number dropped to 58.9 % when a stoma was to be retained. Some 68.8 % would not be put off the operation by a 28-day stay in hospital, but only 19.4 % would be prepared to face a significant risk to their life. Fifty percent would still undergo transplantation even if it did not result in a normal voice, and 47.3 % of respondents thought research money could be better spent on other projects.

Regression testing (Table 3) demonstrated that younger respondents found the prospect of transplantation significantly more appealing than older respon-

Table 4 Questions regarding research priorities and responses (numbers and percentages, displayed as pie charts)

What sorts of research questions other than those related to transplantation do you think we should concentrate on?	Yes	No	Don't know	
How we can prevent laryngeal cancer	224	134	14	
How cancer cells develop and behave	148	211	13	
Use of existing treatments in the best way	122	231	19	
Development of new, less damaging treatments	235	127	10	
How we improve the psychological and social care of people with a laryngectomy	140	221	11	
How we may improve the quality of life e.g. swallowing, speech, cosmetic appearance of people after laryngectomy	212	144	16	

dents for the first four scenarios ($P \leq 0.001$). For the first three scenarios, there was also a trend towards those with more recent operations favouring transplantation compared with those whose operation was some years ago, although this pattern failed to reach significance ($P = 0.02$–0.09). Older patients thought that research would be best directed away from laryngeal transplantation ($P = 0.0001$). Gender had no effect on any of the responses.

Table 4 demonstrates which research topics found popularity among the respondents. The most popular subjects were prevention (60.2%), development of new treatments (63.2%) and optimisation of quality of life (57%). Less popular were molecular biology (39.6%), improvement in psychosocial care (37.6%) and optimisation of existing treatments (32.8%).

Discussion

The patient with carcinoma of the larynx faces a potentially devastating threat to his or her future quality of life. Radical surgery to the upper aerodigestive tract has immediate complications that have been well documented [17] and may serve to obscure in the patient's mind the more significant long-term implications of life with a tracheostomy. This study found that a majority of laryngectomees consider laryngeal transplantation an acceptable alternative to life without a larynx under certain conditions.

The response rate of around 40% is understandably much lower than in those studies involving telephone polls, personal interviews or multiple mailings. Therefore, there is likely to be considerable volunteer bias as

those patients with strong feelings or motivation are more likely to respond. The retrospective nature of the study may also introduce a bias in favour of those with a good outcome from surgery.

The sex and age distribution of the sample is compatible with the known epidemiology of laryngeal carcinoma. The sex ratio has altered from 1/10 (female/male) in the period 1957–1961 to 1/5 in 1977–1981 in the West Midlands [18], probably due to the increased social acceptability of smoking in women in the post-war years. The known peak incidence of cancer of the larynx in the 6th and 7th decades of life [18, 22] agrees well with the mean age of 67 and survival time of 6 years in this sample.

The responses relating to acceptability of transplantation showed a marked relation to the age of the respondent. A recurrent theme amongst the older members of the study was their regret that their age precluded any further surgery, and perhaps the question should have been phrased to suggest the operation as an alternative to their original laryngectomy. Despite this, a figure of 75% approval of the "ideal" operation was obtained. This surprisingly positive result was not substantially diminished by the prospect of a prolonged hospital stay or retention of a stoma for breathing purposes. However, the acceptability of the operation was much reduced by the possibility of significant risk to life, or loss of speech. Thus, any such operation must have a low mortality and result in a reasonable voice quality in order to gain wide acceptance. The prospect appears equally acceptable to both sexes.

There is no doubt that objective measures demonstrate good results from tracheo-esophageal puncture (TEP) and voice prosthesis insertion [2]. Indeed, this method is now the gold standard for rehabilitation of patients after laryngectomy [8, 10, 11]. However, these measures do not take into account the true disability of laryngectomy encountered at the personal level, something that is currently under investigation by the European Study Group on Functional Outcomes after Laryngectomy [16]. Further, TEP uses a muscular pharyngo-esophageal segment as its vibratory source, and this remains a weak imitator of the human vocal cords [14].

Physicians and scientists primarily tend to be interested in basic science whereas patients and the general public are more concerned with matters relevant to clinical practice [5]. As competition for research resources continues to rise, methods of prioritisation of such resources are at a premium. As this exercise must be conducted in a climate of increasing accountability, greater lay involvement in health research is a desirable goal [6, 14, 21]. The present study attempts to address this issue with respect to the area of laryngeal cancer research in general and transplantation in particular.

Nearly 50% of respondents, particularly the younger ones, believed that research resources would be better used in areas other than laryngeal transplantation. The preferred directions of further research included prevention, more benign treatments and improvement to quality of life for the laryngectomee. There was little enthusiasm for the basic sciences or the randomised controlled trial, topics that have yet to grasp the understanding, or perhaps the imagination, of the general public [3]. In fact, lay opinion in medical matters must be treated with caution, as evidenced by the Oregon survey in which cosmetic surgery was regarded as more essential to public health than treatment of open fractures [20]. Nonetheless, the present study addressed a relatively well-informed group whose views are likely to be better formed than those of the general population.

In conclusion, amongst respondents to our survey, there was a strong majority who would find laryngeal transplantation an acceptable procedure. This was particularly so if the procedure was regarded as safe and if a voice could be reliably re-established. By contrast, the persistence of a stoma appeared less important. Younger patients were significantly more likely to favour the procedure. When asked about research, however, many respondents felt that research money might be better spent on other areas, particularly prevention of laryngeal cancer. These results suggest that there is a potential pool of willing recipients should a safe laryngeal transplantation procedure be developed with a high chance of restoring phonation. The views of persons who have had a laryngectomy with regard to laryngeal cancer research should be considered by researchers and funding bodies.

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