

Quality of life after operative treatment of sinonasal inverted papilloma – a prospective study*

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Abstract

Background: Studies assaying morbidity related to sinonasal inverted papilloma (SNIP) and its treatment are lacking. We evaluated how operative treatment of SNIP affects patients' health-related quality of life (HRQoL) and symptoms.

Methods: We prospectively recruited consecutive patients (n=52) operated for SNIP at Helsinki University Hospital, between years 2016 and 2019. In total, 42 patients filled in the 15D, a generic HRQoL instrument and a symptom questionnaire preoperatively and at 1 year and at 2 years postoperatively. The 15D HRQoL scores were compared to those of age- and sex-standardized general population.

Results: Patients' mean baseline score for discomfort and symptoms (one of the 15D dimensions) was significantly better compared to general population, but this difference faded postoperatively. Frequency of epistaxis, nasal obstruction, lowered sense of smell, headache, tinnitus and epiphora decreased significantly during follow-up whereas frequency of numbness of the face or mouth increased. Difference in the mean 15D score of the patients compared with general population was insignificant at baseline and at 1 year and at 2 years postoperatively.

Conclusions: Measured by a generic HRQoL questionnaire, the mean score for discomfort and symptoms deteriorated after operative treatment of SNIP. Despite a relief of many symptoms, care should be taken when operating a benign tumour, as surgery may cause morbidity.

Key words: quality of life, operative treatment, paranasal sinus neoplasms, sinonasal inverted papilloma, symptoms

Introduction

Sinonasal inverted papilloma (SNIP) is a benign epithelial tumour of nose and paranasal sinuses. It is characterized by locally destructive growth, tendency to recur and a potential for malignant transformation ⁽¹⁾. The favoured treatment of SNIP is endoscopic surgical excision ⁽²⁾. SNIP may cause distractive symptoms, such as nasal obstruction, rhinorrhea, epistaxis, hyposmia and headache ⁽¹⁾. Surgical treatment may also result in morbidity ⁽³⁾. Since SNIP is primarily a benign tumour, it is important that the treatment does not cause excessive morbidity. Prospective collection and analysis of patients' health-related quality of life (HRQoL) data provides a tool to assess this. To date, only few studies have evaluated long-term HRQoL after surgery among patients with SNIP and only two of the studies were

prospective ⁽³⁻⁵⁾. Van Samkar and Georgalas found that measured by a disease-specific Sino-nasal Outcome Test-22 (SNOT-22), patients returned to an almost normal quality of life after endoscopic removal of SNIP ⁽³⁾. Derosseau et al. found that measured by 20-item Sino-Nasal Outcome Test (SNOT-20), patients had a significant improvement in overall SNOT-20 scores and rhinologic and sleep subdomain scores after minimally invasive endoscopic resection of SNIP ⁽⁴⁾. Studies on generic HRQoL of patients with SNIP and the data comparison to general population are lacking. Moreover, studies how surgery of SNIP affects patients' symptoms are scarce.

We aimed to study the effect of SNIP and its operative treatment on patients' generic HRQoL and symptoms. Furthermore, we

compared the generic HRQoL results of patients with SNIP to those of general population.

Methods

We prospectively recruited consecutive patients treated for SNIP at the Helsinki University Hospital, Department of Otorhinolaryngology – Head and Neck Surgery, between April 2016 and December 2019. Only patients who had not been operated for SNIP in the past three years were included. The patients completed a questionnaire about their symptoms and a generic HRQoL instrument 15D preoperatively and 1 year and 2 years after the operation. Patients' HRQoL scores were compared to a representative age- and sex-standardized sample of general population obtained from a large national health examination survey ⁽⁶⁾. The study was approved by the Helsinki University Hospital Ethics Committee, and the institutional permission was granted. All patients provided a written informed consent.

15D instrument

Generic quality of life was measured by the 15D instrument, a generic, comprehensive, 15-dimensional, standardized and self-administered measure of HRQoL ⁽⁷⁾. 15D can be used as a profile and single index score measure. The 15D includes 15 dimensions: breathing, mental function, speech (communication), vision, mobility, usual activities, vitality, hearing, eating, excretion, sleeping, distress, discomfort and symptoms, sexual activity, and depression. The respondent chooses for each dimension one of five levels best describing the state of health at the moment (best level = 1; the worst level = 5). The valuation system is based on an application of the multi-attribute utility theory. The single index score (15D score), representing the overall HRQoL on a 0-1 scale (1=full health, 0=being dead) and the dimension level values, reflecting the goodness of the levels relative to no problems on the dimension (=1) and to being dead (=0), are calculated from the health state descriptive system by using a set of population-based preference or utility weights. Mean dimension level values are used to draw 15D profiles for groups ⁽⁷⁾. The minimum clinically important change or difference in the 15D score has been estimated to be ± 0.015 on the basis that people can on average feel such a difference ⁽⁸⁾.

Symptom questionnaire

The symptom questionnaire was created for this study to explore how frequently patients reported symptoms that have been previously associated with SNIP in the literature. The questionnaire included questions about rhinorrhea, epistaxis, nasal obstruction, lowered sense of smell, headache, tinnitus, diplopia, epiphora, facial pain, and numbness of the face or mouth. Patients were asked to respond if they had experienced these symptoms on a four-point grading scale: never, seldom, quite often or often.

Statistical analyses

Statistical analyses were performed with IBM SPSS Statistics software, version 27 (SPSS, Inc., Chicago, IL, USA). Statistical significance of the differences in the means of 15D variables between the patients and age- and sex-standardized general population was tested with independent samples t-test. Within the patient group, paired samples t-test was used to test the statistical significance of differences in the means of variables across time. Spearman's rank correlation coefficient was used to test the strength and direction of a relationship between some 15D variables and symptom variables. P-values ≤ 0.05 were considered statistically significant.

Results

In total, 90 consecutive patients with SNIP were recruited in a larger prospective study published elsewhere ⁽⁹⁾. Of those, 52 consecutive patients were asked to fill in the 15D and a symptom questionnaire. In total, 42/52 patients (80.8%) returned both questionnaires preoperatively and represent the patients in this study (Table 1). Mean age of the 42 patients at baseline was 60.5 years (median 60.0 years, range 31 - 88 years). Of the 42 patients, 6 experienced a recurrent SNIP and 5 of them were re-operated because of their tumour recurrence during 2 years of follow-up (Table 1).

Surgical approach

All 42 patients were operated for their SNIP (Table 1). In vast majority of the patients, the surgery was endonasal endoscopic (39/42, 92.9%). Only three (7.1%) patients were operated in a combination technique (i.e., by an external approach in combination with endoscopes). All the three combination technique operations were accomplished through the canine fossa via a sublabial approach (Caldwell-Luc approach). None of the operations were merely external without the use of endoscopes. Endoscopic medial maxillectomy was performed for 8 (35%) of the 23 maxillary sinus tumours. Two of the patients developed orbital swelling in the recovery room and a lateral canthotomy and cantholysis were performed immediately. One patient developed a cerebrospinal fluid fistula after the operation and was re-operated twice for the fistula (2 days and 11 days after the primary operation). None of the three patients with complications had permanent handicap.

Generic HRQoL, 15D

The mean baseline 15D HRQoL score (0.921) was not statistically significantly different from that of the general population (0.914, $p=0.612$, CI -0.035 - 0.021; Figure 1). At baseline, patients' mean score for sleeping (0.757) was significantly worse compared to that of the general population (0.833, $p=0.043$, CI 0.03 - 0.149). The mean sleeping score remained worse compared to the general population at 1 year and at 2 years after the operation,

Table 1. Demographic and clinical characteristics of the study populations.

Characteristics	Number of patients (%), N=42
Sex	
Female	17 (40.5)
Male	25 (59.5)
Recurrent tumour at first presentation	3 (7.1)
Primary site of the attachment of the tumour*	
Maxillary sinus	23
Ethmoid sinus	8
Middle turbinate	4
Uncinate process	3
Sphenoid sinus	2
Frontal sinus	2
Scull base	1
Surgical approach	
Endoscopic	39 (92.9)
External	0 (0)
Combination	3 (7.1)
Dysplasia at some point during follow-up	14 (33.3)
Malignant transformation	0 (0)
Surgical complication	3 (7.1)
Questionnaires preoperatively	
15D	42 (100)
Symptom questionnaire	42 (100)
Questionnaire at 1 year after operation	
15D	33 (78.6)
Symptom questionnaire	35 (83.3)
Questionnaire at 2 years after operation	
15D	29 (69)
Symptom questionnaire	28 (66.7)
Events during the 1st year of follow-up	
Recurrence	5 (11.9)
Revision surgery	3 (7.1)
Events during 2 years of follow-up	
Recurrence	6 (14.3)
Revision surgery	5 (11.9)

*One patient had a tumour attached to uncinate process and ethmoid sinus.

but the difference was not statistically significant. The difference between the patients' mean sleeping score at baseline and at 1 year and at 2 years after the operation was insignificant. The patients' mean baseline score for discomfort and symptoms (0.872) was statistically significantly better compared to the general population (0.808, $p=0.016$, CI -0.116 - -0.013), but this difference faded at 1 year and at 2 years after the operation. The patients' mean score for discomfort and symptoms deteriorated significantly at 1 year after the operation compared to the baseline ($p=0.043$, CI -0.143 - -0.003) and the result remained stable at 2 years after the operation. The mean score of mental function of the patients (0.951) was significantly better compared to the general population (0.893) at baseline ($p=0.014$, CI

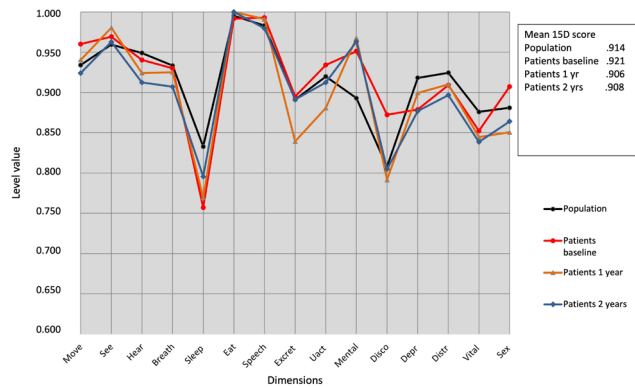


Figure 1. Mean scores in the 15D instrument. Move, mobility; See, vision; Hear, hearing; Breath, breathing; Sleep, sleeping; Eat, eating; Excret, excretion; Uact, usual activities; Mental, mental function; Disco, discomfort and symptoms; Depr, depression; Vital, vitality; Sex, sexual activity; yr, year; yrs, years.

-0.104 - -0.012) and the difference remained at 1 year ($p<0.001$, CI -0.124 - -0.043) and at 2 years ($p=0.001$, CI -0.124 - -0.033) after the operation. The difference in the patients' mean scores for 15D dimensions at 1 year and at 2 years after the operation was not statistically significant. That is, the results remained stable after the first and the second postoperative year. The mean 15D HRQoL score of the patients was not statistically significantly different compared with the general population at 1 year and at 2 years after the operation.

Symptom questionnaire

The frequency of epistaxis ($p=0.005$), nasal obstruction ($p<0.001$), lowered sense of smell ($p<0.001$), headache ($p=0.009$), tinnitus ($p=0.005$) and epiphora ($p=0.006$) decreased significantly at 1 year after the operation compared to the baseline and this difference was stable at 2 years after the operation (Figure 2a). In contrast, the frequency of numbness of the face or mouth increased significantly at 1 year after the operation compared to the baseline ($p=0.021$) and the result remained stable at 2 years after the operation (Figure 2b). Among the patients with worsened facial numbness, 1 patient had a sphenoidal tumour without infraorbital nerve injury and 6 patients had a maxillary sinus tumour. Among these 6 patients, 3 tumours were mentioned to attach near or at the site of infraorbital nerve. Among 2 of the 6 patients, maxillary sinus mucosa was extensively removed (endoscopically in 1 patient and via sublabial approach in 1 patient). One of the patients with a maxillary sinus tumour had endoscopic medial maxillectomy without a mention of the infraorbital nerve. Patients reporting diplopia had no orbital complications.

Comparison of 15D and symptom questionnaire results

At baseline, the frequency of epistaxis ($r=-0.391$, $p=0.011$) and



Figure 2a. Frequency (%) of patients' symptoms at baseline and postoperatively. Y-axis, Percentage of respondents; n, Number of the patients who responded.

the frequency of epiphora ($r=-0.415$, $p=0.006$) correlated negatively with the sleeping difficulties, i.e., the higher the frequency, the worse the sleeping difficulties. At 1 year after the operation, the frequency of nasal obstruction correlated to the worsening of discomfort and symptoms ($r=-0.364$, $p=0.041$). Similarly, the frequency of diplopia correlated to the worsening of sleeping difficulties at 1 year after the operation ($r=-0.391$, $p=0.025$).

Discussion

To our knowledge, this is the first study to compare generic HRQoL of patients with SNIP to that of a general population.

At baseline, the patients had a significantly better mean score on the dimension of discomfort and symptoms compared to the general population measured with the 15D instrument, but interestingly this difference evened at 1 year and at 2 years after the operation. Hytönen et al. had similar findings of deteriorating scores in their study on HRQoL of patients that underwent septoplasty⁽¹⁰⁾. An explanation for this could be that surgery as such may cause morbidity. As SNIP per se is a benign tumour, the treatment should not cause excessive harm. Of the 42 patients with SNIP, 5 experienced a recurrence during the first year of follow-up and 1 during the second year of follow-up (Table

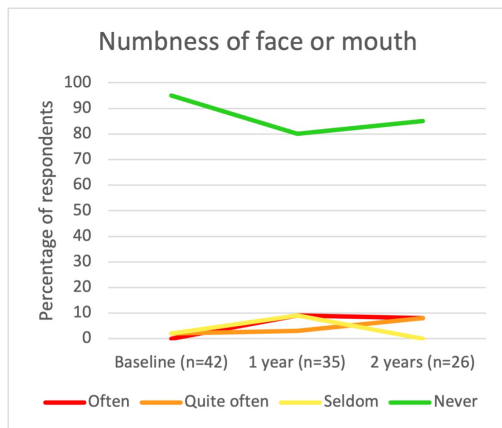


Figure 2b. Frequency (%) of patients' symptoms at baseline and postoperatively. Y-axis, Percentage of respondents; n, Number of the patients who responded.

1). Of these patients 3 had a revision surgery during the first follow-up year and 2 had a revision surgery during the second follow-up year. Thus, the low rates of tumour recurrence and revision surgery may not significantly impact the results. These results highlight the importance of elaborate patient counseling on potential disadvantages before operation. Patients in our study scored poorly on the 15D dimension of sleeping, which may partly explain the decline on the dimension of discomfort and symptoms. The poor scores on the sleeping dimension may be related to the symptoms caused by the tumour, for example nasal obstruction.

The decrease in the frequency of epistaxis, nasal obstruction, lowered sense of smell, headache, tinnitus and epiphora at 1 year after the operation compared to the baseline may reflect the benefits of the tumour removal. In contrary, increase in the frequency of numbness of the face or mouth at 1 year after the operation compared to the baseline, may result from an injury to the infraorbital nerve at the operation.

Comparing the 15D dimensions and patients' symptoms we found a negative correlation of frequency of epistaxis and epiphora with sleeping difficulties at baseline. Epistaxis may wake up and thus increase sleeping difficulties. At 1 year after the operation there was a correlation between the frequency of nasal obstruction and the worsening of discomfort and symptoms. This may be explained by discomfort in breathing with obstructed nose. Our patients' mean score of discomfort and symptoms deteriorated at 1 year after the operation compared to the baseline. Furthermore, at 1 year after the operation the frequency of diplopia correlated to the increasing difficulty on the 15D dimension of sleeping. Possible mental stress caused by diplopia might disturb sleep.

Van Samkar and Georgalas retrospectively evaluated the

quality of life of 27 patients with SNIP comparing postoperative SNOT-22 scores to those of a general population ⁽³⁾. The median follow-up in their study was 6 years and they concluded that patients returned to an almost normal quality of life after surgery. Preoperatively the most frequent symptom was nasal obstruction and postoperatively a need to blow the nose. Similarly, nasal obstruction was preoperatively the most frequent of the symptoms analysed in our study. SNOT-22 has been used in SNIP-studies. However, at the time this study began SNOT-22 was validated only as a rhinosinusitis questionnaire and not in Finnish language, and therefore it was not applied. Thus, we made a symptom questionnaire for this study.

Derousseau et al. prospectively studied the quality of life of patients treated for sinonasal tumour 2 years after minimally invasive endoscopic resection using SNOT-20 ⁽⁴⁾. They included 72 patients with sinonasal malignancy and 32 patients with SNIP served as controls. In their study, patients with SNIP had a significant improvement in overall SNOT-20 scores and rhinologic and sleep subdomain scores at 6 months, and the improvement remained stable at 2 years. In our study, the patients' mean sleeping score measured by the 15 D instrument did not improve significantly at 1 year or at 2 years after the operation.

Deckard et al. prospectively studied quality of life of 71 patients with sinonasal and skull base neoplasms using SNOT-20, Anterior Skull Base Questionnaire (ASBQ) and EuroQol (EQ-5D) questionnaire ⁽⁵⁾. They found in a mean follow-up of 14.5 months that patients with malignant tumours (n=32) had significantly worse scores compared to patients with benign tumours (n=39, including 15 patients with SNIP), but they did not report in detail the changes in scores among patients with SNIP. In contrast, we analysed data on HRQoL and symptoms particularly in patients with SNIP.

A small study population and a non-validated symptom questionnaire were limitations of our study. The questionnaires were given to patients during outpatient visits or sent to them. Due to ethical considerations, we were unable to ask for missing questionnaires by phone. Furthermore, the time interval for the experienced symptoms was not marked precisely in the symptom questionnaire. Patients may have experienced other life events besides SNIP that may have contributed to the HRQoL during follow-up. However, the events related to SNIP (recurrences and revisions) occurred with a similar frequency during the first and the second year of follow up. Moreover, a prospective consecutive setting and follow up of two years are the strengths of the study.

Conclusions

The frequency of nasal obstruction, lowered sense of smell, epis-

taxis, headache, tinnitus and epiphora decreased after operative treatment of SNIP compared to the baseline during the follow-up. In contrast, the frequency of numbness of the face or mouth increased. Patients' mean 15D dimension score for discomfort and symptoms deteriorated during the follow-up. These findings emphasize that we should aim at the removal of tumour that is extensive enough meanwhile avoiding unnecessary morbidity as SNIP per se is a benign tumour.

Authorship contribution

Study concept, design: SV LMA, HS. Statistical analysis and writing: SV, HS. Manuscript review: SV, LMA, MH, ML, HS.

Conflicts of interest

The authors have no conflicts of interest to disclose.

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SUPPLEMENTARY MATERIAL

Quality of Life Questionnaire (15d®)

Please read through all the alternative responses to each question before placing a cross (x) against the alternative which best describes your present health status. Continue through all 15 questions in this manner, giving only one answer to each.

QUESTION 1. MOBILITY

- 1 () I am able to walk normally (without difficulty) indoors, outdoors and on stairs.
- 2 () I am able to walk without difficulty indoors, but outdoors and/or on stairs I have slight difficulties.
- 3 () I am able to walk without help indoors (with or without an appliance), but outdoors and/or on stairs only with considerable difficulty or with help from others.
- 4 () I am able to walk indoors only with help from others.
- 5 () I am completely bed-ridden and unable to move about.

QUESTION 2. VISION

- 1 () I see normally, i.e. I can read newspapers and TV text without difficulty (with or without glasses).
- 2 () I can read papers and/or TV text with slight difficulty (with or without glasses).
- 3 () I can read papers and/or TV text with considerable difficulty (with or without glasses).
- 4 () I cannot read papers or TV text either with glasses or without, but I can see enough to walk about without guidance.
- 5 () I cannot see enough to walk about without a guide, i.e. I am almost or completely blind.

QUESTION 3. HEARING

- 1 () I can hear normally, i.e. normal speech (with or without a hearing aid).
- 2 () I hear normal speech with a little difficulty.
- 3 () I hear normal speech with considerable difficulty; in conversation I need voices to be louder than normal.
- 4 () I hear even loud voices poorly; I am almost deaf.
- 5 () I am completely deaf.

QUESTION 4. BREATHING

- 1 () I am able to breathe normally, i.e. with no shortness of breath or other breathing difficulty.
- 2 () I have shortness of breath during heavy work or sports, or when walking briskly on flat ground or slightly uphill.
- 3 () I have shortness of breath when walking on flat ground at the same speed as others my age.
- 4 () I get shortness of breath even after light activity, e.g. washing or dressing myself.
- 5 () I have breathing difficulties almost all the time, even when

resting.

QUESTION 5. SLEEPING

- 1 () I am able to sleep normally, i.e. I have no problems with sleeping.
- 2 () I have slight problems with sleeping, e.g. difficulty in falling asleep, or sometimes waking at night.
- 3 () I have moderate problems with sleeping, e.g. disturbed sleep, or feeling I have not slept enough.
- 4 () I have great problems with sleeping, e.g. having to use sleeping pills often or routinely, or usually waking at night and/or too early in the morning.
- 5 () I suffer severe sleeplessness, e.g. sleep is almost impossible even with full use of sleeping pills, or staying awake most of the night.

QUESTION 6. EATING

- 1 () I am able to eat normally, i.e. with no help from others.
- 2 () I am able to eat by myself with minor difficulty (e.g. slowly, clumsily, shakily, or with special appliances).
- 3 () I need some help from another person in eating.
- 4 () I am unable to eat by myself at all, so I must be fed by another person.
- 5 () I am unable to eat at all, so I am fed either by tube or intravenously.

QUESTION 7. SPEECH

- 1 () I am able to speak normally, i.e. clearly, audibly and fluently.
- 2 () I have slight speech difficulties, e.g. occasional fumbling for words, mumbling, or changes of pitch.
- 3 () I can make myself understood, but my speech is e.g. disjointed, faltering, stuttering or stammering.
- 4 () Most people have great difficulty understanding my speech.
- 5 () I can only make myself understood by gestures.

QUESTION 8. EXCRETION

- 1 () My bladder and bowel work normally and without problems.
- 2 () I have slight problems with my bladder and/or bowel function, e.g. difficulties with urination, or loose or hard bowels.
- 3 () I have marked problems with my bladder and/or bowel function, e.g. occasional 'accidents', or severe constipation or diarrhea.
- 4 () I have serious problems with my bladder and/or bowel function, e.g. routine 'accidents', or need of catheterization or enemas.
- 5 () I have no control over my bladder and/or bowel function.

QUESTION 9. USUAL ACTIVITIES

- 1 () I am able to perform my usual activities (e.g. employment, studying, housework, free- time activities) without difficulty.
- 2 () I am able to perform my usual activities slightly less effectively or with minor difficulty.
- 3 () I am able to perform my usual activities much less effectively, with considerable difficulty, or not completely.
- 4 () I can only manage a small proportion of my previously usual activities.
- 5 () I am unable to manage any of my previously usual activities.

QUESTION 10. MENTAL FUNCTION

- 1 () I am able to think clearly and logically, and my memory functions well
- 2 () I have slight difficulties in thinking clearly and logically, or my memory sometimes fails me.
- 3 () I have marked difficulties in thinking clearly and logically, or my memory is somewhat impaired.
- 4 () I have great difficulties in thinking clearly and logically, or my memory is seriously impaired.
- 5 () I am permanently confused and disoriented in place and time.

QUESTION 11. DISCOMFORT AND SYMPTOMS

- 1 () I have no physical discomfort or symptoms, e.g. pain, ache, nausea, itching etc.
- 2 () I have mild physical discomfort or symptoms, e.g. pain, ache, nausea, itching etc.
- 3 () I have marked physical discomfort or symptoms, e.g. pain, ache, nausea, itching etc.
- 4 () I have severe physical discomfort or symptoms, e.g. pain, ache, nausea, itching etc.
- 5 () I have unbearable physical discomfort or symptoms, e.g. pain, ache, nausea, itching etc.

QUESTION 12. DEPRESSION

- 1 () I do not feel at all sad, melancholic or depressed.
- 2 () I feel slightly sad, melancholic or depressed.
- 3 () I feel moderately sad, melancholic or depressed.
- 4 () I feel very sad, melancholic or depressed.
- 5 () I feel extremely sad, melancholic or depressed.

QUESTION 13. DISTRESS

- 1 () I do not feel at all anxious, stressed or nervous.
- 2 () I feel slightly anxious, stressed or nervous.
- 3 () I feel moderately anxious, stressed or nervous.
- 4 () I feel very anxious, stressed or nervous.
- 5 () I feel extremely anxious, stressed or nervous.

QUESTION 14. VITALITY

- 1 () I feel healthy and energetic.
- 2 () I feel slightly weary, tired or feeble.
- 3 () I feel moderately weary, tired or feeble.
- 4 () I feel very weary, tired or feeble, almost exhausted.
- 5 () I feel extremely weary, tired or feeble, totally exhausted.

QUESTION 15. SEXUAL ACTIVITY

- 1 () My state of health has no adverse effect on my sexual activity.
- 2 () My state of health has a slight effect on my sexual activity.
- 3 () My state of health has a considerable effect on my sexual activity.
- 4 () My state of health makes sexual activity almost impossible.
- 5 () My state of health makes sexual activity impossible.

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