

Effect of Shunt Surgery on Life Satisfaction and Health-related Quality of Life in Patients with Idiopathic Normal Pressure Hydrocephalus

Degree Project in medicine



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SAHLGRENKA ACADEMY

EFFECT OF SHUNT SURGERY ON LIFE
SATISFACTION AND HEALTH-RELATED
QUALITY OF LIFE IN PATIENTS WITH
IDIOPATHIC NORMAL PRESSURE
HYDROCEPHALUS

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ABBREVIATIONS

ADL – Activities of the daily living

CSF – Cerebrospinal fluid

CNS – Central nervous system

CT – Computerised tomography

EQ5D-5L – EuroQol group 5 dimensions 5 levels

HRQoL – Health-related quality of life

ICP – Intracranial pressure

iNPH – Idiopathic normal pressure hydrocephalus

ITT – Intention to treat

LiSat-11 – Life satisfaction checklist-11

LS – Life satisfaction

MR – Magnetic Resonance

VAS – Visual analogue scale

ABSTRACT

Title: Effect of shunt surgery on life satisfaction and health-related quality of life in patients with idiopathic normal pressure hydrocephalus

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BACKGROUND

Idiopathic normal pressure hydrocephalus (iNPH) is a condition causing gait- and balance disturbance, neurocognitive impairment and urinary incontinence in the elderly. After treatment with shunt surgery, up to 80% of patients improve. Life satisfaction (LS) has not been reported in patients with iNPH, but their health-related quality of life (HRQoL) is poorer than in the healthy population, improving after shunt surgery. However, HRQoL has only been scarcely studied in these patients.

AIM

To research LS and HRQoL in patients with iNPH before and after shunt surgery and to explore how these measures are related to how patients are dependent on others in daily life and severity of clinical symptoms.

METHODS

One hundred and twenty-two iNPH-patients (49 female; mean age 74 years) had their clinical symptoms evaluated according to the iNPH-scale, dependence on others according to the modified Rankin Scale (mRS) and LS, and HRQoL using the LiSat-11 and EQ5D-5L- questionnaires at baseline and three months post-surgery.

RESULTS

Before surgery, 32% were satisfied with life as a whole, increasing to 47% after ($p = .004$). Patients also improved in leisure, self-care, physical, and psychological health LS ($p < .001$). Satisfied patients scored higher on the iNPH-scale ($p = .002$). Postoperative improvement on EQ5D-5L 0-100 visual analogue scale was seen in 73% of patients ($p < .001$). Dependent patients (mRS 3-5) had poorer LS ($p = .008$) and lower grades on the EQ5D-5L visual analogue scale ($p = .003$) than independent patients (mRS 0-2).

CONCLUSION

A majority of iNPH-patients experience their life as a whole unsatisfactory. After treatment both LS and HRQoL improves but around 50% of the patients are still unsatisfied with their life as a whole which should be assessed further. Pronounced symptoms and dependence are associated with worse LS and HRQoL, implying that altered function plays an essential role regarding these measures.

KEY WORDS

Idiopathic normal pressure hydrocephalus; shunt surgery; life satisfaction; health-related quality of life

BACKGROUND/INTRODUCTION

THE VENTRICULAR SYSTEM

The ventricular system is a system of cavities within the brain in which the cerebrospinal fluid (CSF) circulates. Anatomically the ventricular system is divided into four different spaces, or ventricles, numbered one to four. The first and second ventricles are called the lateral ventricles and are paired cavities located in each hemisphere. The lateral ventricles are connected via two interventricular openings (foramina) to the medially located third ventricle which, through the narrow cerebral aqueduct, transcends into the fourth ventricle positioned posterior to the brain stem. There are three openings from the fourth ventricle to the external subarachnoid space (between the arachnoid and pia mater) which surrounds both the brain and the spinal cord. (1)

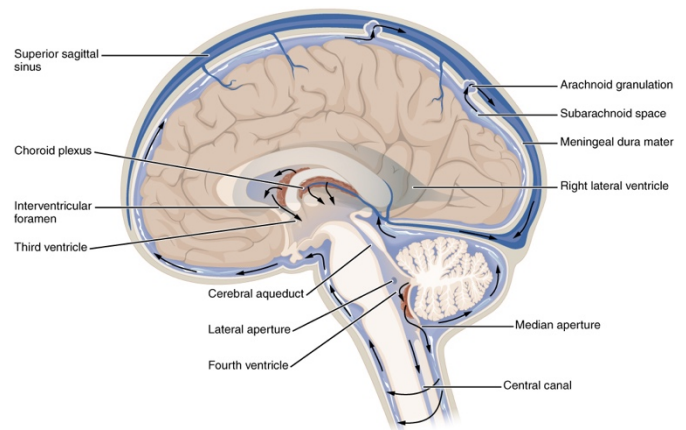


Figure 1: Anatomical picture of the ventricular system. The arrows represent the direction of the cerebrospinal fluid-circulation (3).

The main part of the CSF is produced within the ventricles in the so-called choroid plexus, a plexus of specialised ependymal cells, and then circulates in the ventricular system and the external subarachnoid space (1, 2). The main part of the CSF-absorption is thought to happen in the arachnoid villi or granulations of the cranium and spinal cord (2). The ventricular system and the circulation of CSF is illustrated in figure 1 (3). CSF has several functions, among them a cushioning effect on the central nervous system (CNS). It also plays an important role in the cerebral homeostasis (2).

HYDROCEPHALUS

The dynamics of the cerebrospinal fluid (CSF) are essential in the condition called hydrocephalus. There are a several different classifications of hydrocephalus, often based on the physiology of the CSF circulation (4). One classification first described by Dandy WE (5)

divides the forms hydrocephalus into communicating or not communicating depending on if there is a connection between the different compartments for the CSF or not. Hydrocephalus can also be parted into two groups depending on if the CFS-pressure is elevated or normal. Lastly, the etiology can be used to divide hydrocephalus-patients into two different classes: secondary, if the cause is known, or idiopathic hydrocephalus (4). Causes for secondary hydrocephalus include bleeding, infection, head trauma and tumours (6).

IDIOPATHIC NORMAL PRESSURE HYDROCEPHALUS (INPH)

Idiopathic normal pressure hydrocephalus (iNPH) is a syndrome with communicating enlarged ventricles even though the intracranial pressure is normal. This results in symptoms of gait- and balance- disturbance, neurocognitive dysfunction and urinary incontinence. (7) The condition was first described by S. Hakim and R. D. Adams in 1965 (8).

INPH is the most commonly occurring form of hydrocephalus in adults with a prevalence of 0.2% in patients aged 70-79 years old and 6% in the elderly population, 80 years and older, according to a study from 2014 (9). There is no difference in prevalence between men and women according to the same study. A Swedish study from 2005 investigated the rate of surgical treatments performed on patients with different forms of hydrocephalus and the resulting incidence was 3.4 surgeries per 100,000 adults (6). This result could indicate that the syndrome today is greatly under-diagnosed, which is in line with the results from a systemic literature review focusing on iNPH by Rubén Martín-Láez et al in 2015 (10).

PATHOPHYSIOLOGY

INPH is believed to be caused by a disturbance in the dynamics of the CSF. The reason for the unbalance and why it manifests with the characteristic symptoms is still not fully known (7). The main theory used to explain hydrocephalus with normal pressure today is that the absorption of CSF in the arachnoid villi is defective which in turn leads to affected CSF-dynamics (6). In a study by Jaraj et al aiming to explore the risk factors for iNPH, factors such

as hypertension and diabetes mellitus was associated with iNPH, indicating that the vascular system could play an important role in the syndrome's pathophysiology (11).

CLINICAL PICTURE

iNPH is characterised by a tetrad of symptoms, initiated by a progressive gait-disturbance that gradually develop with an addition of the other symptoms: balance-disturbance, urinary incontinence and neurocognitive impairment. Presence of all symptoms are not mandatory to receive the diagnosis (7) but in most cases at least 3 out of the 4 symptom domains are affected (12) and gait disturbance is generally considered obligatory according to diagnostic criteria (13). To suspect the disorder, the iNPH symptoms should have been present for 6 months (14).

The classic iNPH-patient has a broad-based gait-pattern (12). The gait disturbance is typically symmetric and resembles neurodegenerative disorders like Parkinson's disease (7), displaying difficulties with gait initiation, shuffling and a need to take multiple steps when turning (7, 14). The balance- disturbance is characterised by a tendency to fall backwards (15), often a forward-leaning stance and a difficulty of balance that worsens with loss of visual stimuli (13). Furthermore, the cognitive impairment in iNPH includes several different symptoms such as amotivation, daytime sleepiness, psychomotor symptoms and disturbance of memory and executive function. The effects of the cognitive disturbance resemble that of other forms of dementias. Finally, the urinary symptoms include urinary urgency and incontinence, sometimes also fecal incontinence. (14)

CLINICAL INVESTIGATION

The clinical investigation contains a combination of a neurological examination and neuroimaging with a computerised tomography (CT) or preferably magnetic resonance imaging (MRI) (7). The diagnosis is determined using the international guidelines for iNPH (13) and the judgement is based on the results from the examinations and knowledge of the

patients' medical history. A central part of the investigation involves exclusion of other explanations to the patient's symptoms and if another cause is found this should usually be treated first. Beyond these examinations it is usually recommended to test the dynamics of the CSF by doing a lumbar puncture to measure the opening pressure or in difficult cases add one of the following: tap test (drainage of 30-50 ml CSF and assessing clinical improvement), external lumbar drainage and/or CSF infusion testing. These tests can both show if the patient has affected dynamics of the CSF and also predict the response to shunt surgery. (7)

However, the sensitivity to select shunt responders is low (16).

TREATMENT

The treatment that has been proven to give the best results, on patients with iNPH, today is shunt surgery, more specifically ventriculo-peritoneal shunt surgery, where the cerebrospinal fluid (CSF) is usually steered from the ventricle-system to the abdomen. In a few cases the CSF is instead led from the ventricle-system to the right atrium (7). Using this treatment method, up to 80% of the patients improve in all of the domains of the tetrad (gait and balance, cognition and urinary control) (17).

LIFE SATISFACTION

Life satisfaction (LS) is a measurement based on patients' evaluation of their own contentment with life, depending on the level of fulfilment they feel considering their personal goals and achievements. LS can be used to measure enjoyment with life as a whole but also to judge patients' satisfaction with different aspects of life. (18)

LiSat-11 (Life Satisfaction Questionnaire 11) is a questionnaire used to measure LS in general and in 10 domains of life such as ADL (activities of daily living), somatic health and psychological health. The scale has six levels (1-6) where low values represent poor satisfaction with life and high values represent the opposite. (19)

LS according to LiSat-11 has been studied in many different disease categories. A study on LS in patients with Parkinson's disease showed that both depressive symptoms and general self-efficacy are significantly associated with LS, depressive symptoms having a negative association with high LS and general self-efficacy having a positive association with high LS (20). When studying long-term LS in patients with traumatic brain injuries (TBI) most participants were reasonably satisfied with life, all-though when compared to a Swedish reference sample a significant difference could be seen in LS, the reference sample scoring higher than the TBI-patients (21). Life satisfaction according to LiSat-11 has not yet been reported studied in patients with iNPH.

HEALTH-RELATED QUALITY OF LIFE

Health-related quality of life (HRQoL) is a phenomenon describing experienced health according to different aspects of life such as physical, psychological and social health.

HRQoL focuses on the influence a patients' disease has on their capability to fulfil a normal role. This differs from LS which focuses on personal needs and feeling of fulfilment (18).

How patients perceive their HRQoL is subjective why this, if possible, should be assessed by the patients themselves (22).

The EQ5D (EuroQol 5 Dimensions) is a questionnaire constructed by the EuroQol group in 1990 (23) which is generally used to measure HRQoL in patients with different diseases (22). In the EQ5D-5L health related quality of life is graded in five different dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has five levels (1-5), where a low score corresponds to a high HRQoL and a high score corresponds to a low HRQoL. In addition to this the EQ5D-5L has a visual analogue scale (VAS) where the patients score their HRQoL between 0 and 100. (24)

HRQoL has been studied in patients with iNPH before and in a study using EQ5D-3L (three levels/dimension) iNPH patients self-reported HRQoL before shunt surgery was lower when

being compared to an EQ-index for the normal population (24). In the same study a significant increase in HRQoL was seen in patients with iNPH after shunt surgery, 83% reporting improved HRQoL, almost reaching levels for healthy individuals.

Junkkari et al researched HRQoL in iNPH-patients using the 15D-scale (15 dimensions/five grades) in 2015 and found that iNPH-patients reported their HRQoL significantly lower than healthy patients. These levels were in agreement with those in patients with other neurological syndromes (25). In another study by the same group, the HRQoL one year after shunt-surgery was evaluated using the same scale (15D) and improvement in HRQoL was seen in less than fifty percent of the patients (26). The latter study resulted in a complementary study investigating the discrepancy between self-assessed quality of life and the functional outcome in iNPH-patients after shunt-surgery. This showed that patients with a poor basic condition and comorbidities pre-operatively might have a smaller chance to improve in HRQoL after shunt-surgery even though the functional outcome is improved (27).

AIM

The aim of this study was to evaluate how patients with iNPH experience their own disease in terms of life satisfaction and HRQoL. With this study we also wanted to investigate how these patients consider their well-being is affected when treated with shunt-surgery. Specific research questions included: how iNPH patients experience their life satisfaction according to LiSat-11, how they experience their health-related quality of life according to EQ-5D-5L, how both these parameters change after shunt surgery and lastly how these measures are affected by the severity of the clinical symptoms, and by the patients' ADL-dependence on others.

MATERIAL AND METHODS

DATA COLLECTION PROCEDURES

This project is part of a larger two-centre interventional study, with researches blinded to interventions, investigating the effects of physical exercise after shunt-surgery in iNPH, a cooperation between the Sahlgrenska and Linköping university hospitals. Data was collected from both these clinics. Power was calculated based on primary outcome measures and expected changes in LiSat-11 and EQ5D-5L. All patients diagnosed with iNPH, according to international guidelines (13) and subjected to shunt surgery between 1 January 2016 and June 2018, were invited to participate in the study. Patients with ≤ 16 points on the mini mental state examination (MMSE) (28) and/or inability to walk 10 meters with or without support or who were considered unable to participate in the physical exercise program for other obvious reasons such as severely impaired vision were excluded from participation in the study. Since this project aims to investigate the patients' health related quality of life (HRQoL) and life satisfaction (LS) a patient's failure to reply to at least one of the two questionnaires at baseline was a complementary exclusion criterion. Baseline-characteristics of the final 122 patients in the study are demonstrated in table 1.

The patients were randomised into two different groups (A and B). Both groups were given a written advice for physical self-exercise after surgery. Patients in group A were subjected to an additional physical exercise program with a physiotherapist two times a week for 12 weeks after surgery. A total of 49% were randomised to group A and 51% to group B. The medical staff involved in the evaluation of the patients were not informed about which group the patients randomised into. Due to time limits, in this project, effect of physical training was not studied: patient data was analysed regardless of randomisation.

According to iNPH guidelines, the clinicians divide patients into three different categories based on the likelihood of an iNPH-diagnosis: probable, possible and unlikely. The different

categories are based on a combination of typical clinical history and neurological symptoms together with typical neuroradiological findings (13). Here, both probable and possible cases are included. The patients' clinical symptoms were evaluated by a standardised clinical assessment before and three months after shunt surgery. The iNPH scale (29) was used to score symptoms pre- and postoperatively and the difference between the post- and the preoperative iNPH scale score was used as a measure of clinical outcome, improvement defined as an increase of at least 5 points. The overall level of function and independence was scored according to the modified rankin scale (mRS) (30) pre- and postoperatively. Vascular risk factors (hypertension, diabetes, history of stroke, cardiovascular disease) were registered as present or absent.

Patients' life satisfaction was evaluated by the LiSat-11 questionnaire (19) and health-related quality of life by the EQ5D-5L questionnaire (23) at baseline and three months after surgery. All patients also underwent an MRI of the brain pre- and postoperatively and had a lumbar puncture at the preoperative examination.

Table 1: Demographic data of 122 iNPH patients at baseline

Age (mean, range)	74 (44-89)
Female (% , n)	40 (49)
Duration of symptoms in months (median, range)	33 (2-254)
Vascular risk-factors (% , n)	
Diabetes	31 (38)
Hypertension	67 (82)
History of stroke	6 (7)
Cardiovascular disease	22 (26)
MMSE (mean, SD)	26 (\pm 3)
Dependent (% , n)	53 (63)

SD = Standard deviation. MMSE = Minimental state examination. Dependent = 3-5 points on the modified Rankin Scale

MISSING VALUES

A total of 129 patients were primarily included in the study. Two of the participants were later not accepted for surgery why these two should not have been included in the first place.

Another five patients were excluded because they had not answered any of the two questionnaires before surgery leaving a total of 122 patients in the study. In all, 102 patients were available for postoperative evaluation: 2 patients had passed away before time of follow-up; 12 patients were excluded because of complications to shunt-surgery (9 patients because of subdural hematomas; 2 patients because of shunt-dysfunctions and 1 patient because the shunt had to be extirpated due to a shunt infection); 3 patients were excluded because of other severe diseases that came in between, and 3 patients chose to end their participation in the study. One patient had a myocardial infarction and one was diagnosed with cancer of the uterus during the study-period but both patients were considered able to continue the study because the diseases were believed not to affect the patient measures in a substantial way. The missing values are illustrated in figure 2.

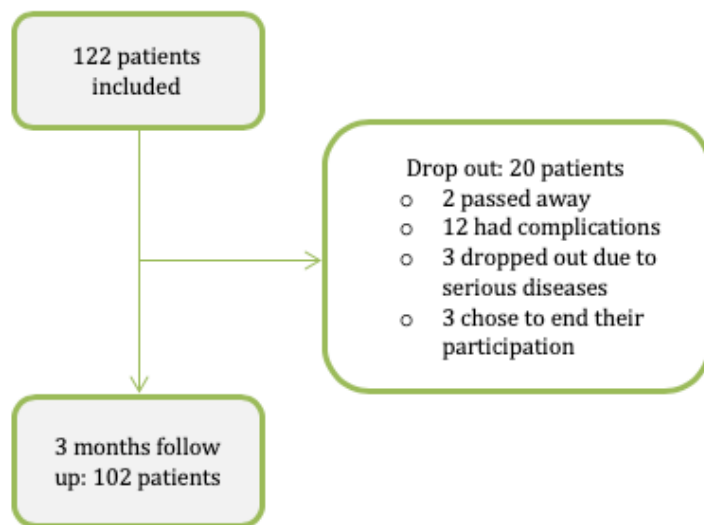


Figure 2: Flow chart on the exclusion of patients during the study period.

CLINICAL VARIABLES

The severity of the disease was estimated using the iNPH-scale which is a scale grading the four symptoms of the iNPH-tetrad: gait, balance, urinary and cognitive dysfunction as a score ranging from 0 to 100 where 100 equals normal function and 0 maximal symptom burden (29). The mRS is a scale judging the patients' daily function and dependence on others. The

scale has 7 levels where 0 means that the patient has normal function and 6 means that the patient is deceased (30). In this study the mRS-scale 0-5 was used and dichotomised patients into two groups: independent (0-2 points) or dependent (3-5 points).

Life satisfaction (LS) was assessed using the LiSat-11 questionnaire consisting of 11 items where item 1 is a general question regarding life as a whole. Each question can be answered on a scale from 1 to 6 where 1 is the worst possible life satisfaction and 6 is the best possible life satisfaction (19). For analysis the answers were dichotomised into unsatisfied (1-4 points) or satisfied (5-6 points). Overall life satisfaction was judged according to item one, life as a whole, on the LiSat-questionnaire. An increase with one point was defined as an improvement. All other items were evaluated one by one.

Health-related quality of life (HRQoL) was evaluated using the EQ5D-5L which is a questionnaire measuring HRQoL in five different domains of life: mobility, self-care, usual activities, pain/discomfort and anxiety/depression on a scale from one to five, one representing good HRQoL and five poor (31). A mean-value of all scores on the questionnaire was computed on each patient and was named EQSum. The EQ5D-5L also has a visual analogue scale (VAS) where the participants estimate their HRQoL from 0 to 100, where 0 is the worst possible quality of life whereas 100 is the best. Improvement was defined as ≥ 5 -point increase on EQ-VAS and ≥ 1 -point increase on the 5 different items.

STATISTICAL ANALYSIS

Since both the EQ5D-5L and the LiSat-11 are ordinal scales, non-parametric statistics were applied to the data. Mann-Whitney U test was used to investigate differences between groups for independent variables such as differences in scoring between men and women and differences in scoring depending on results on mRS before and after shunt surgery. The percentages of satisfied patients on the LiSat-11 (5-6 points) were calculated for each question before and after surgery. To measure changes over time (results before surgery

compared to 3 months after), sign-test was used for the dichotomised values of LiSat and mRS. To measure changes over time on the iNPH-scale, EQ5D-5L VAS and EQSum, Wilcoxon signed rank test was used. The two analyses measuring changes over time only included the group of patients who had answered pre- and postoperatively meaning that the group investigated over time is a bit smaller than the entire sample. The proportion of patients who improved in their scoring after surgery was calculated for each of the items in the EQ5D-5L (≥ 1 -point increase for items and ≥ 5 points on EQ-VAS) and for item 1 on the LiSat-11 (≥ 1 -point increase).

To investigate whether there was an association between the patients iNPH-score and their life satisfaction (item 1), a comparison was made between satisfied and unsatisfied with regard to their iNPH-score pre- and post-operatively using Mann-Whitney U test. To compare HRQoL and iNPH-scale scores, Spearman correlation coefficient was calculated between self-estimated health (EQ5D-5L VAS) and iNPH-score. This correlation was calculated postoperatively as well. Using Mann-Whitney U test a comparison was made between the improved and unimproved groups on EQ5D-5L VAS and LiSat item 1 and their scores on the iNPH-scale postoperatively. Two-tailed p-values were calculated and <0.05 was considered significant. The statistical analysis was made in IBM SPSS Statistics for MacOS, version 25, Armonk, NY: IBM Corp.

ETHICS

The study was approved by the regional ethics committee in Linköping (Dnr 2015/250-31). Written and informed consent was obtained from all patients and/or their relatives.

RESULTS

BASELINE

Baseline mean score on the iNPH-scale was 56 points (± 16 ; \pm SD) (table 2), women generally had lower scores (53 ± 15 for women; 59 ± 16 for men, $p = .036$). Altogether, 53% of the participants were judged as dependent on others using the mRS-scale.

LIFE SATISFACTION BEFORE SURGERY

Thirty-two percent of the patients were satisfied with life as a whole (item one) before shunt surgery. LiSat item scores are displayed in table 2. The LiSat-11 item with the lowest share of satisfied patients was somatic health (8%). Women generally scored lower than men on the questions about finance (4 ± 1 for women; 5 ± 1 for men; median \pm IQR, $p = .002$) and partner relationships (4 ± 1 for women; 5 ± 1 for men, $p = .002$), otherwise no sex differences were seen. The answering frequency was considerably lower on the questions related to the participants vocational situation and sexual life why these two questions were excluded from further analysis. Patients who were categorised as dependent on others on the mRS-scale graded their overall LS lower than patients who were categorised as independent (4 ± 1 for dependent; 4 ± 1 for independent; median \pm IQR, $p = .008$). Patients satisfied with life as a whole scored higher on the iNPH-scale than those not satisfied (63 ± 14 for satisfied; 53 ± 16 for unsatisfied; mean \pm SD, $p = .002$).

HEALTH-RELATED QUALITY OF LIFE BEFORE SURGERY

In average, the patients graded their health-related quality of life as 52 (± 19 ; \pm SD) out of 100, using the visual analogue scale. The mean of EQSum before surgery was 2.5 (± 0.7). No significant difference was seen between the sexes in scoring on EQ-VAS, EQSum and on the different items on EQ5D-5L. Dependent patients scored higher on EQSum (2.8 ± 0.7 for dependent; 2.2 ± 0.6 ; mean \pm SD, for independent, $p < .001$) and lower on EQ-VAS (47 ± 18 for dependent, 57 ± 19 for independent, $p = .003$) than patients who were counted as independent.

There was a significant difference between the dependent and independent groups on four out of the five items on the EQ5D-5L: mobility ($p = .001$), self-care ($p < .001$), usual activities ($p < .001$), pain/discomfort ($p = .044$). The exception was the question about anxiety and depression where no significant difference was seen between the groups ($p = .167$). A correlation was found between the patients VAS-values and iNPH-score, $R_s = 0.21$ ($p = .024$).

CHANGES AFTER SURGERY

After shunt-surgery 81% of the patients improved ≥ 5 points on the iNPH-scale. The percentage of patients who were dependent on others decreased from 53% before surgery to 33% after ($n = 97$, $p < .001$) (table 2). Dependent patients were associated with poorer values on item 1 of LiSat-11 (4 ± 1 for dependent; 4 ± 1 for independent; median \pm IQR, $p = .012$) and on EQ-VAS (56 ± 19 for dependent; 71 ± 17 for independent; mean \pm SD, $p = .001$) than independent patients after surgery as well. The values before and after surgery are demonstrated in table 2 below.

Table 2: Results pre-operatively and 3 months post-operatively

	Pre-op (n=122)	Missing values	Post-op (n=102)	Missing values
iNPH-score (mean, SD)	56 (± 16)		72 (± 16) ***	
Dependent (% , n)	53 (63)	2	33*** (32)	4
LiSat-11 (median, IQR)				
Life as a whole	4 (± 2)	2	4 (± 1) **	7
Economy	5 (± 1)	3	5 (± 1)	6
Leisure	4 (± 2)	4	4 (± 1) ***	7
Contacts	4 (± 2)	2	5 (± 1)	7
ADL	4 (± 2)	2	5 (± 2) ***	6
Family life	5 (± 2) (n=110)	12	5 (± 2) (n=89)	13
Partner relationship	5 (± 2) (n=99)	23	5 (± 2) (n=81)	21
Somatic health	3 (± 2)	2	4 (± 2) ***	7
Psychological health	4 (± 2)	1	5 (± 1) ***	7
EQ5D-5L (median, IQR)				
Mobility	3 (± 2)	1	2 (± 1)	8
Self-care	1 (± 1)	1	1 (± 0)	7
Usual activities	3 (± 2)	1	2 (± 2)	8
Pain/Discomfort	3 (± 1)	4	2 (± 1)	7
Anxiety/Depression	2 (± 1)	2	1 (± 1)	8
Self-estimated health (mean, SD)	52 (± 19)	2	67 (± 19) ***	9
EQSum (mean, SD)	2.5 (± 0.7)	5	1.9 (± 0.7) ***	9

Dependent – 3-5 points on the mRS-scale. LiSat-11 – Life Satisfaction questionnaire 11. EQ5D-5L – EuroQol 5 dimensions 5 levels. Self-estimated health – score on the 0-100 visual analogue scale on EQ5D-5L. EQSum – mean value of all scores on the questionnaire for each patient. ADL = Activities of daily living. SD = Standard deviation. IQR = Interquartile range.

* represents a significant change 3 months after surgery. ** = $p < .01$. *** = $p < .001$. n = number of patients with family or partner relationship.

LIFE SATISFACTION

The patients scored their overall satisfaction with life (item 1) higher after surgery than before (n= 93, p =.004) (figure 2).

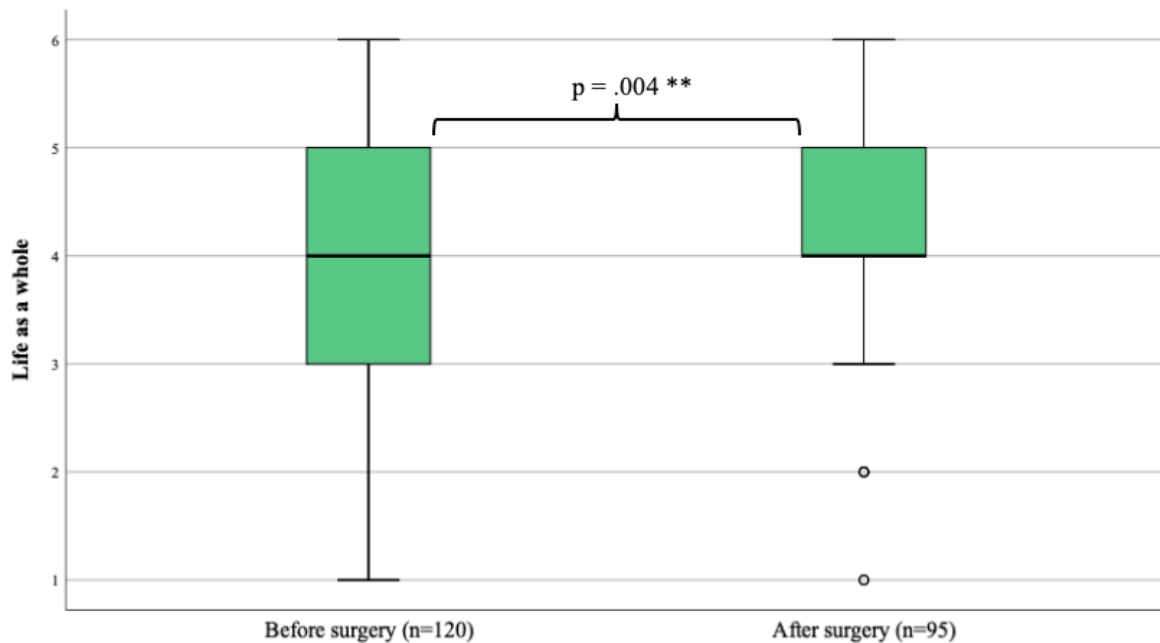


Figure 2: Box-plot of median value and interquartile range on Item 1 on Life Satisfaction questionnaire 11 pre- and post-operatively.

In excess of item 1, a significant increase after surgery was also seen on four other items: leisure situation (n= 91, p <.001), ability to manage my self-care (n= 94, p <.001), physical health (n= 93, p <.001) and psychological health (n= 94, p <.001) (table 2). The proportion of satisfied patients, according to item 1, after surgery was 47%. The percentage of satisfied patients on each item before and after surgery are demonstrated in table 3 below.

Table 3: Proportion of satisfied patients in % on the LiSat-11 pre- and post-operatively

	Pre-op (n=122)	Missing values	Post-op (n=102)	Missing values
Life as a whole	32 (n =38)	2	47** (n =45)	7
Financial situation	54 (n =64)	3	65 (n =62)	6
Leisure situation	22 (n =26)	4	47*** (n =45)	7
Contacts	40 (n =48)	2	54 (n =51)	7
ADL	33 (n =40)	2	62*** (n =59)	6
Family life	64 (n =70)	12	71 (n =63)	13
Partner relationship	69 (n =68)	23	74 (n =60)	21
Somatic health	8 (n =10)	2	35*** (n =33)	7
Psychological health	33 (n =40)	1	55*** (n =52)	7

*LiSat-11 – Life Satisfaction Questionnaire 11. Satisfied – scores between 5-6 on the LiSat-11 questionnaire. ADL = Activities of daily living. * represents significant change 3 months after surgery. * represents a significant change 3 months after surgery. ** = $p < .01$. *** = $p < .001$.*

A total of 33% improved at least one point on item 1 after surgery, but this group did not score higher on the iNPH-scale than patients who were not improved on item 1 ($p = .065$).

However, similarly to before surgery satisfied patients were associated with higher scores on the iNPH-scale (77 ± 15 for satisfied; 70 ± 16 for unsatisfied; mean \pm SD, $p = .001$).

HEALTH-RELATED QUALITY OF LIFE

After shunt surgery, patients estimated their HRQoL to be higher than before surgery on EQ-VAS ($n = 91$, $p < .001$) (figure 3). A positive correlation was found between the patients' VAS-values and iNPH-score, $R_s = 0.43$ ($p < .001$).

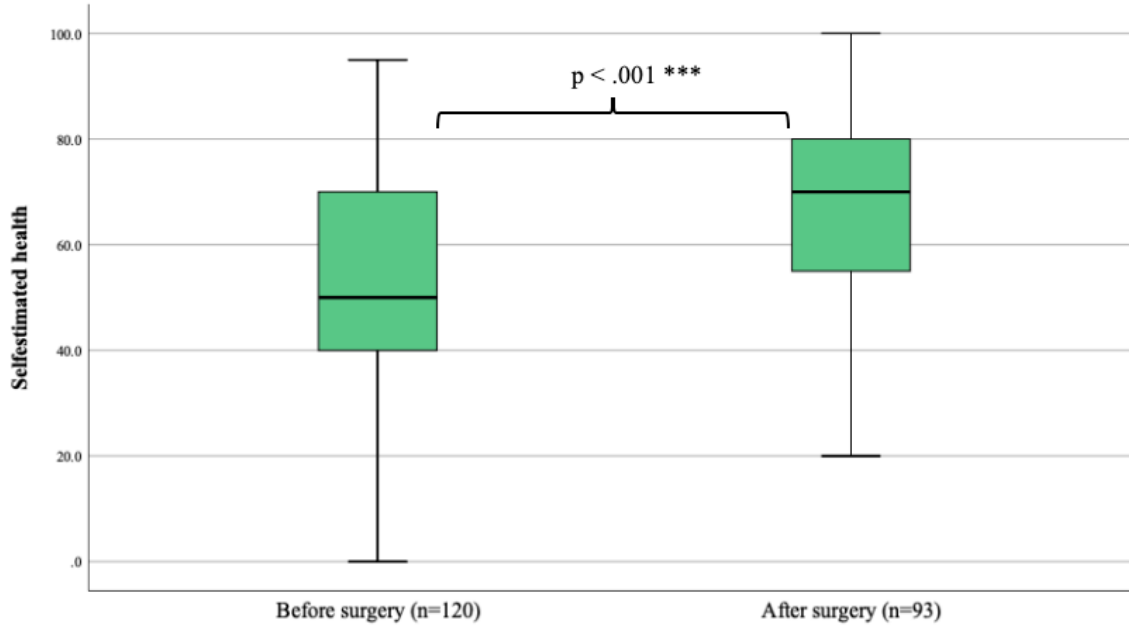


Figure 3: Box-plot of median value and interquartile range on the 0-100 visual analogue scale on EuroQol 5 dimensions 5 levels pre- and post-operatively. Self-estimated health = VAS-value.

Also, the mean of the EQSum-values improved after surgery to 1.9 (± 0.7), $n = 88$, $p = <.001$ (table 2). Seventy-three percent of the patients improved their score on the VAS-scale with at least 5 points post-operatively. The percentages of improved patients, improvement being defined as an increase with at least 1 point, on the different items on the EQ5D-5L-questionnaire are presented in table 4 below.

Table 4: Percentage of improved patients after surgery on EQ5D-5L-items

	Post-op (n=102)	Missing values
Mobility	66 (n =61)	9
Self-care	39 (n =37)	8
Usual activities	58 (n =54)	9
Pain/Discomfort	47 (n =43)	11
Anxiety/Depression	49 (n =45)	10

EQ5D-5L – EuroQol 5 Dimensions 5 Levels.

DISCUSSION

DISCUSSION OF THE RESULTS

This study attempted to research life satisfaction and health-related quality of life in patients with idiopathic normal pressure hydrocephalus before and 3 months after shunt-surgery using the LiSat-11 and EQ5D-5L -questionnaires and also to explore how these measures are related to how patients are dependent on others in daily life and severity of clinical symptoms.

Our main finding was that only 32% of iNPH patients were satisfied with life as a whole before surgery. Although the patients improved significantly concerning their LS, 53% were still not satisfied with their life as a whole after surgery. Shunt surgery also had a positive effect on HRQoL, mean EQ-VAS increasing from 52 out of 100, to 67 after surgery. Lower scores of LS and HRQoL was noted in patients who were dependent on others. For patients with higher severity of clinical symptoms, there was also a connection to poorer scores on LS and HRQoL.

A total of 81% of the patients who participated in the follow-up improved with at least 5 points on the iNPH-scale. In accordance with these results, previous studies have demonstrated that between 65-84% of iNPH patients improve after shunt surgery (17, 24, 32).

LIFE SATISFACTION

This study set out with the aim of assessing LS in patients with iNPH and our results indicate that the patients do not feel content with life as a whole. When studying LS in a healthy Swedish reference sample 70% scored between five (satisfied) and six (very satisfied) on item one (19). Here, only 32% of the patients in our study were satisfied before surgery and 47% after, which implies that iNPH patients are less satisfied with life as a whole compared with healthy patients. Comparable results have been seen on patients with stroke where only 47,5% of stroke patients <75 years were satisfied with life as a whole one year after stroke debut in a study by Carlsson et al from 2002 (33), and 47% of younger (18-55 years old) stroke patients

were satisfied with life as a whole 8-36 months after stroke in a study by Rödning et al from 2010 (34). A possible explanation to the dissatisfaction after surgery for iNPH may be that the patients have high expectations on the treatment, resulting in a feeling of disappointment after surgery, even though a decreased symptom burden has been seen. Further causes could be coexisting depression, or experience of insufficient support to compensate for functional impairments and assist in daily life activities. In addition, the LS might be altered by presence of comorbidities affecting everyday life, but for example also non-clinical factors such as economic situation, partner relationships and family life which might be hard to influence with treatment. Similar to minor improvement in LS after surgery, patients' activity shows only minor changes after surgery (35).

The answering-frequency was lower on the questions about vocational situation and sexual life which could be partly explained by the fact that this patient group usually have passed the age of retirement, beyond the fact that sexual life can be seen as a sensitive subject. Women were generally less satisfied with their economy and partner relationships than men. These results contradicts those for the Swedish reference sample, where no significant difference could be seen between the sexes on these questions but instead on the questions about ADL and contact with friends and acquaintances, where women scored higher than men (19).

The current study found that iNPH patients were the most dissatisfied with their somatic health both before and after surgery, with only eight percent satisfied patients before surgery, increasing to 35% after. It is interesting to note that the main part of iNPH patients are dissatisfied with their physical health all though the majority of the patients improve on the iNPH-scale. As mentioned earlier, the proportion of unsatisfied patients might be explained by a disappointment in relation to the result of the surgery, based on high expectations on the treatment. The biggest improvement could be seen regarding ADL (self-care), where the share of satisfied patients went from 33% to 62%. Patients estimated LS on psychological health increased from 33% to 55% satisfied patients. However, iNPH patients LS values are still

lower than in a Swedish reference sample on each of these questions (19). The observed increase in LS on questions about ADL, somatic and psychological health could possibly be attributed to a decreased symptom burden after shunt surgery.

An important and clinically relevant finding was that iNPH patients ADL-dependence on others was associated with poorer LS both before and after surgery. This is in accordance to a study on LS in patients with another chronic neurological condition, Parkinson's disease, where a connection could be seen between poor overall self-efficacy and dissatisfaction with life as a whole (20). In our study LS-rates also had a relation to the patients' scores on the iNPH-scale, low scores being related to lower values on item 1 (life as a whole), and vice versa. This could be seen as further confirmation that the symptoms of the condition have an effect on patients' satisfaction with life. However, there was no difference in iNPH-scale scores between the improved and not improved group regarding satisfaction with life as a whole. This might be an indication that LS, as a measure, takes more aspects into account than clinical symptoms alone. To our knowledge LS has not been studied in iNPH patients before, why further studies are warranted to see if findings can be replicated.

HEALTH-RELATED QUALITY OF LIFE

Another aim of the study was to assess iNPH patients HRQoL, to which focus will be moved in the upcoming section. The average score on 0-100 VAS-scale (EQ-VAS) was 52 (± 19 ; \pm SD) before surgery. This result coincides relatively well with earlier studies where the mean of iNPH patients pre-operative VAS-values has stretched between 55-60 points (24, 32). After shunt surgery EQ-VAS values increased to a mean of 67 points, which is a smaller outcome than in the previously mentioned studies, where HRQoL increased to 80 points after surgery. The pre-operative EQ-VAS values in our study match those of Golicki et al in their study investigating HRQoL in stroke patients, where the mean baseline EQ-VAS was 54 points (31).

It is not that surprising that the greatest improvement in HRQoL was seen on the question about mobility (66% improved), since disturbed gait and balance are both symptoms of iNPH. Furthermore, the least share of improved patients was seen on the question about self-care, which is quite interesting in view of that the largest delta-improvement in LS was seen on the item about ADL.

A relation was found between HRQoL and ADL-dependence, ADL-dependence being associated with lower HRQoL-scores (EQ-VAS). This relation has been found in iNPH-patients before. Petersen et al (24) saw a positive correlation between EQ-VAS scores and the patients' independence, using the functional independence measure. An interesting finding was that mRS-score was not connected to patients' feelings of anxiety and depression. To our knowledge, this has not been noticed before. This result may be explained by the fact that these symptoms are not purely physical and that even though the patients' might feel limited by their psychiatric symptoms, this affects the clinicians' evaluation of the patients' dependence less than physical symptoms. EQ-VAS-values correlated positively with iNPH-scale scores weakly before and stronger after surgery. The observed correlation shows that patients with more symptom burden have poorer HRQoL. The fact that the correlation strengthens after surgery could possibly imply that there is something affecting EQ-VAS before surgery that we might have managed to eliminate partly with the treatment. In that case this could lead to a clearer connection between the clinical symptoms and HRQoL. There are several possible examples of factors that could be relevant, for example a presence of depressive symptoms such as amotivation and apathy, which could influence the patients' sense of their other symptoms before surgery, and which might improve after surgery, leading to a clearer evaluation. On the other hand, these results could also be affected by the patients' expectations, being affected by a hopefulness before surgery and a feeling of discouragement after. The relation between HRQoL and iNPH-score has been reported earlier, in the aforementioned study by Petersen et al (24) a correlation between improvement in HRQoL

and iNPH-score was found, improved scores on EQ-VAS being correlated with an increase of the score on the iNPH-scale.

THE DIFFERENCE BETWEEN HRQoL AND LS

In our study, there was an obvious numeral difference in improvement between HRQoL (75% improved) and LS (33% improved). A theory to why a larger share of the patients improved their HRQoL than their LS could be that HRQoL focuses more on function or easily put: “what you can do”. In contrast to HRQoL, LS focuses more on the patients’ subjective satisfaction with what they can do. Taking this into consideration the HRQoL improvement may possibly be more connected to the functional outcome whereas LS shows that there is more to take in account for the patients to feel satisfied. However, it is important to approach this thought with caution, since LS is still a very new measure in this patient-group. Junkkari et al researched which factors were associated with the discrepancy between self-assessed quality of life and the functional outcome in iNPH-patients (27). In future investigations, it might be interesting to do a similar study on LS, researching factors that affect LS to further distinguish patients who improve only functionally from those who improve in function as well as LS after treatment.

STRENGTHS AND WEAKNESSES

One of the limitations of this study is the fact that the measurements are subjective and can be interpreted differently depending on the patient. Further, a patients’ scoring on these instruments can be affected by influences that might vary between days. This could also be affected by the cognitive function which is often altered in patients with iNPH. To reduce the risk of the cognitive status affecting the results all patients with ≤ 16 points on MMSE were excluded from the study. Even if patients were allowed to get help from a close relative, we cannot rule out that some patients might have had difficulties using the instruments adequately. Further, assessments were made by the patients’ in their homes, minimising bias

caused by hospital staff. This study is part of an intervention study investigating the effects of physical exercise after shunt surgery. We cannot rule out that the patients included, all willing to take part in a three-months' physical exercise program, differ from the general iNPH population with regard to the measures of LS and HRQoL presented here, i.e. that the study design introduces a selection bias. However, the inclusion of patients was consecutive, and the vast majority of eligible patients accepted participation in the study. Further, clinical characteristics of patients are expected and compatible with those of other study populations why we believe that the results reported are valid.

All though there are a few limitations to this study there are also several strengths. All patients were diagnosed according to international guidelines. The group-size is large, the patients were consecutively included, evaluated and diagnosed systematically and the procedures were standardised using well-known and well-tested instruments. Although we had to exclude patients for different reasons, we have no reason to believe this have any effect on the results reported here, apart from reducing statistical power. In all, we think results reported here are valid.

CONCLUSIONS AND IMPLICATIONS

A majority of iNPH-patients experience their life as a whole unsatisfactory. When treated with shunt surgery, 81% improve clinically but around half of the patients are still unsatisfied. INPH-patients also have a poor HRQoL which improves in 75% of the patients post-operatively. Worse LS and HRQoL is associated with poorer ADL function and more pronounced symptoms.

These results seem to suggest a need for deeper understanding of what lies behind patients' life satisfaction and proposed interventions aiming specifically to further increase LS and HRQoL in these patients.

POPULÄRVETENSKAPLIG SAMMANFATTNING

I hjärnan finns det ett sammanhängande system av hålrum i vilket hjärn- och ryggmärgsvätska cirkulerar. När dynamiken av hjärn- och ryggmärgsvätskan i detta system är påverkad ger det upphov till en vidgning av hjärnans hålrum i kombination med en klassisk symptombild bestående av gång- och balanssvårigheter, urininkontinens och påverkad intellektuell funktion. Syndromet uppstår hos den äldre populationen och i dagsläget missas det ofta, vilket gör att för få patienter får diagnosen. Den mest effektiva behandlingen är operation där man skapar en förbindelse mellan hålrummen i hjärnan och bukhålan i vilken överflödigt hjärn- och ryggmärgsvätska kan tömmas. Trots att detta är en sjukdom som förekommer hos många äldre har livstillfredsställelse fortfarande inte undersökts på denna patientgrupp överhuvudtaget och hälsorelaterad livskvalitet har endast undersökts ett fåtal gånger.

Med denna studie hoppas vi få en större förståelse för hur dessa patienter själva upplever sin livskvalitet och tillfredsställelse med hjälp av två olika skattningsskalor, en för respektive område. Ett annat mål är att undersöka hur dessa mått förändras efter operation och hur dessa mått påverkas av sjukdomsburda samt hur hjälpberoende patienterna är.

Denna studie är ett samarbete mellan två medicinska center (Sahlgrenska och Linköpings universitetssjukhus) med 122 patienter som har fått diagnosen enligt de nationella riktlinjerna för sjukdomen och som har planerats för den tidigare beskrivna typen av förbindelseoperation mellan januari 2016 och juni 2018. Patienternas kliniska symptom och hjälpberoende värderades före och tre månader efter operation. Vid samma vårdtillfällen skattades även livstillfredsställelse och hälsorelaterad livskvalitet av patienterna med hjälp av de två olika skattningsskalorna. 102 patienter var kvar vid uppföljningen efter 3 månader.

Efter operation förbättrades 81% av patienterna i sina symptom. Andelen som var nöjda med livet som helhet var 32% innan operation och ökade till 47% efter. Patienterna förbättrades också inom nöjdhet med fritid, själv-vård, fysisk och psykisk hälsa. Operationen medförde även en förbättring i livskvalitet hos 73%. Patienter som var beroende av andras hjälp för att klara sig i det vardagliga livet hade generellt sett sämre livsnöjdhet och livskvalitet än de som klarade sig i vardagslivet själva. De nöjda patienterna hade ofta mindre symptombörda. Ett samband sågs även mellan mindre symptombörda och bättre livskvalitet.

En majoritet av denna patientgrupp är missnöjda med livet som helhet. Då de behandlas med kirurgi förbättras 81% kliniskt, men en större del av patienterna är fortsatt missnöjda. Dessa patienter har också dålig livskvalitet, vilken förbättras hos 75% av patienterna efter operation. Sämre livsnöjdhet och livskvalitet är dessutom associerat med bristande självständighet och större sjukdomsbörda. Den här studien talar för att det finns ett behov av åtgärder som fokuserar på att specifikt förbättra livsnöjdhet och livskvalitet hos denna patientgrupp.

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