

Comparative study on the effect of education and patient awareness before open heart surgery on delirium rates after surgery

Seyed Mohammadreza Amouzegar Zavareh¹, Mohammad Sadegh Pour Abbasi², Seyed Alireza Amouzegar Zavareh³, Masoud Latifi-Pour^{4*}

¹ Atherosclerosis research center, Clinical Sciences Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran

² Assistant professor of Cardiovascular Surgery Kashan University of Medical sciences, Kashan, Iran

³ Kashan University of Medical Sciences, Kashan, Iran.

⁴ Chemical Injuries Research Center and Systems Biology and Poisonings Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran

*Corresponding Author: Masoud Latifi-Pour, Chemical Injuries Research Center and Systems Biology and Poisonings Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran. Email: latifi3t@gmail.com, Phone: 09121097556.

Received 2025-01-04; Accepted 2025-07-03; Online Published 2025-12-01

Abstract

Introduction: Delirium following heart surgery can lead to adverse effects. This study examined the effectiveness of educating patients and raising their awareness before open-heart surgery to reduce the incidence of delirium afterward.

Methods: This prospective study was conducted with patients undergoing open heart surgery at Ayatollah Beheshti Hospital in Kashan and Baqiyatallah Hospital in Tehran. The data collection included demographic information and the Mini-Mental State Examination (MMSE). In the intervention group, the researcher provided patients with a pre-prepared educational video the night before surgery, which covered information about their condition, treatment methods, and what to expect until discharge. The MMSE test was administered to the patients before surgery and again at 18 to 24 hours and 24 to 48 hours after surgery. The collected data were analyzed using SPSS version 26 software.

Results: In a study of 67 patients who underwent cardiac surgery, 18 patients (26.8%) developed delirium afterward. Among these, 13 patients were in the control group (23.38%), while five were in the intervention group (15.15%). The data analysis revealed a significant difference between the intervention and control groups ($P=0.004$).

Conclusion: While education decreased the occurrence of delirium after cardiac surgery in the intervention group, factors like increasing age and higher education levels also contributed to a reduced incidence of delirium.

Keywords: Delirium, surgery, education.

Citation: Amouzegar Zavareh S-M, Sadegh Pour Abbasi M, Amouzegar Zavareh S-A, Latifi-Pour M. Comparative study on the effect of education and patient awareness before open heart surgery on delirium rates after surgery. Int J Travel Med Glob Health, 2025;13(4):242-247. doi: 10.30491/ijtmgh.2025.497925.1451.

Introduction

Delirium is a sudden and temporary cognitive impairment that affects brain function. It is commonly observed in patients undergoing cardiac surgery and is linked to severe complications. Despite its high incidence and the seriousness of these complications, there is currently no effective treatment available to prevent delirium from occurring¹. There is no difference in the incidence of complications between treated and untreated individuals. Therefore, this study was designed to prevent delirium. It is a comparative study examining the relationship between the level of education and awareness of patients

before open-heart surgery and the level of delirium they experience afterward². The pattern of disease prevalence is changing, transitioning from infectious diseases to lifestyle disorders. As a result, hospital admissions and surgeries are on the rise. Cardiovascular diseases are becoming more common among older individuals who have various comorbidities, including high blood pressure, diabetes, and renal failure. These patients often require surgical intervention³⁻⁴. Over the past few decades, advancements in surgical techniques and postoperative care have resulted in a decrease in mortality

rates following cardiac surgery. However, patients who undergo this type of surgery may still experience significant pain, sleep disturbances, postoperative delirium (POD), and postoperative cognitive decline (POCD). These complications can lead to more extended hospital stays and increased healthcare costs. Additionally, postoperative pain and sleep disturbances can directly affect the development of delirium and hinder cognitive recovery. If these complications become long-term, they can hurt a patient's quality of life⁵.

Patient safety is a crucial issue highlighted by the World Health Organization across all countries. It is also a primary focus of clinical governance aimed at creating "patient safety-friendly hospitals."⁶ Patient safety protects individuals from harmful or adverse events during medical treatment. Delirium can jeopardize patient safety by heightening the risk of falls, increasing mortality rates, and prolonging hospital stays⁶. Delirium is one of the oldest known medical disorders and is characterized by an acute and temporary disturbance in brain function. This condition leads to decreased attention and cognition, resulting in significant cognitive impairment, fluctuations in mental status, impaired awareness, inattention, and disorganized thinking. Delirium typically has an abrupt onset, occurring over hours to days, and is marked by a fluctuating nature along with a deterioration of consciousness and reduced clarity of awareness of the surrounding environment⁷.

The causes of delirium are complex and multifactorial; its occurrence results from modifiable and non-modifiable factors⁸. Multiple studies have indicated that several factors can affect patients after cardiac surgery, particularly as they relate to pain management. These factors include increasing age, visual and hearing impairments, depression, and the use of permanent catheters, physical restraints, infections, dehydration, sleep disturbances, hypoxia, and pain relief. Pain is a modifiable factor and a complex, subjective experience among these. An unpleasant sensory and emotional condition may arise from actual or potential tissue damage⁹.

With over 230 million procedures requiring anesthesia performed worldwide, the number of procedures for patients over 65 steadily increases. After 2020, this age group is expected to undergo the most procedures. If these trends continue, millions of elderly patients could be at risk of developing postoperative cognitive dysfunction (POCD) in the coming years. This underscores the importance of addressing POCD at the individual and societal levels, highlighting the need for significant efforts in this area¹⁰.

The incidence of POD can vary based on the type of surgery performed. One study reports that delirium rates range from 3% to 47% after cardiac surgery, 10% after major general surgery, and 24% to 50% after orthopedic surgery. These instances typically occur within the first three days following surgery. Among elderly patients, between 30% and 80% develop delirium after major surgery. Additionally, 30% to 40% experience early postoperative cognitive dysfunction (POCD), and 10% to 15% develop late POCD. Alarming, only 4% of elderly patients with delirium fully recover by the time of discharge, and 80% continue to exhibit residual cognitive impairment six months later¹¹.

Delirium after cardiac surgery is associated with several complications, including an extended length of stay in both the hospital and the intensive care unit. It can lead to an increased mortality rate, which ranges from 22% to 76%, comparable to the mortality rates seen in sepsis or myocardial infarction. Additionally, delirium negatively affects 6-month survival rates and the ability to wean patients off ventilators. Other complications include the development of nosocomial pneumonia, an increased risk of recurrence of delirium, falls, urinary incontinence, skin disorders, and permanent disabilities. It can also result in a lack of improvement in cognitive status¹².

Delirium in patients following cardiac surgery is linked to a higher incidence of postoperative complications. For example, the rate of postoperative respiratory failure is 9.32% for those with delirium compared to 7% for those without. Additionally, sternal instability occurs in 5.7% of patients with delirium, while only 1.9% of patients without delirium experience this issue. The need for sternal re-correction is also greater in those with delirium, at 4.6%, compared to 4.1% for those without. These complications often result in more extended hospital stays. Therefore, recognizing and preventing delirium is crucial for improving patient outcomes¹³. Complications from delirium persist in at least 20% of patients aged 65 and older, significantly increasing hospital costs per patient¹⁴. This introduction aims to educate and inform patients about the potential for delirium after open heart surgery.

Methods

This prospective was conducted with patients undergoing open heart surgery at Ayatollah Beheshti Hospital in Kashan and Baqiyatallah Hospital in Tehran. The data collection included demographic information and the Mini-Mental State Examination (MMSE). In the intervention group, the researcher provided patients with a pre-prepared educational video the night before surgery, which covered information about their condition,

treatment methods, and what to expect until discharge. The MMSE test was administered to the patients before surgery and again at 18 to 24 hours and 24 to 48 hours after surgery. The collected data were analyzed using SPSS version 26 software.

This study will include patients aged 55 to 75 years who fall under ASA classes I and II. Eligible patients must have a MMSE score of 23 or higher and be scheduled for elective open-heart surgery with an anesthesia duration of 4 to 6 hours. The following criteria must also be met: patients should not have any known psychological illnesses, should not be using antipsychotic, antianxiety, or antidepressant medications, and must have no history of brain surgery, stroke, elevated ICP, brain trauma within the past 12 months, alcoholism, substance abuse, or sensitivity to anesthetics. Additionally, patients must be willing to cooperate throughout the study.

To determine the sample size, 29 patients would be needed for each group to achieve a difference of 1.5 in MMSE scores between the two groups, with a power of 80% and a 5% probability of Type I error. This calculation accounts for two standard deviations in MMSE scores; therefore, a total of 30 patients was considered for each group.

$$Z_{1-\alpha/2}=1.96$$

$$Z_{1-\beta}=.84$$

$$n = \frac{(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta})^2 [P_1(1-P_1) + P_2(1-P_2)]}{(P_1 - P_2)^2}$$

The study involved randomly assigning patients into two groups: one receiving training (case group) and another not receiving training (control group), determined by a random number table.

Inclusion criteria

1. Elective surgery for ASA class I and II patients
2. Surgeries that will last 4-6 hours.

Exclusion criteria

1. Emergency surgery
2. ASA class higher than II
3. Preoperative MMSE score less than 23
4. History of known psychological illness
5. Use of antipsychotic, antianxiety, and antidepressant medications
6. History of brain surgery, stroke, high ICP, brain trauma in the past 12 months, alcoholism and substance abuse, and sensitivity to anesthetic drugs
7. Participants may be unwilling to cooperate and engage in the study.

This study studied 60 patients (two groups of 30) aged 55-75 with ASA class I and II who met the inclusion criteria. In the intervention group, patients were fully informed by the researcher the night before the operation about their disease, treatment method, and expected recovery until discharge through a pre-prepared educational video. After securing an appropriate peripheral vein and placing an arterial line, patients in both groups underwent standard monitoring, which included ECG, pulse oximetry, body temperature measurement, and capnography, as well as invasive blood pressure (IBP) monitoring. Following this, all patients were preoxygenated with 100% oxygen for 3 minutes. Anesthesia was induced with 0.1 mg/kg of midazolam and 10 µg/kg of fentanyl administered intravenously. To promote muscle relaxation, 0.2 mg/kg of cis-atracurium was used. After intubation, patients were mechanically ventilated, and the accuracy of the diagnosis was confirmed through chest auscultation and capnography. To monitor central venous pressure and establish a suitable central venous catheter, a CVLine was inserted via the right jugular vein.

To maintain anesthesia, the following medications were administered: 0.07 µg/kg/min of fentanyl, 0.5 µg/kg/min of midazolam, and 0.8 µg/kg/min of atracurium.

Standard monitoring protocols were put in place, which included pulse oximetry, a three-lead ECG, non-invasive blood pressure (NIBP) monitoring, heart rate (HR) measurement, bispectral index (BIS) assessment, and end-tidal carbon dioxide (ETCO₂) monitoring. Additionally, invasive monitoring for blood pressure and central venous pressure was established. These measurements were recorded every 5 minutes.

At the end of the procedure, all patients were transferred to the open-heart intensive care unit. If their vital signs and arterial blood gas analyses were stable and there was no excessive drainage, patients were able to regain consciousness and undergo extubation within 4 to 6 hours following the procedure.

For patients with a pain VAS score exceeding 3, intravenous morphine was administered for analgesia. The patient's cognitive function was assessed using the three-stage MMSE questionnaire. The first assessment was conducted 12 hours prior to surgery, while the second and third assessments took place between 18-24 hours and 42-48 hours after surgery, respectively. The MMSE questionnaire was administered in a calm environment while the patient was lying on the bed. Each questionnaire took approximately 15 minutes to complete.

The MMSE included questions assessing orientation, attention and calculation, recall, language skills,

repetition, perception, reading comprehension, following instructions, and the ability to construct sentences and write. The cognitive functions of patients in both studied groups were compared using the results from the preoperative test. A decrease of 20% or more in cognitive function was classified as postoperative cognitive dysfunction POCD ¹⁵.

All participants signed the consent form. After receiving approval for the research, the code of ethics was obtained and registered with the Ethics Committee of Kashan University of Medical Sciences and Health Services under ID IR.KAUMS.MEDNT.REC.1400.133. Consent form was received from all participants.

The data were analyzed using descriptive and inferential statistics with SPSS-26 software. The Mann-Whitney test was applied to two-level variables, while the Kruskal-Wallis and Wilcoxon tests were utilized for variables with three or more levels. The significance level was set at 0.05.

Results

In this study, 33 participants (49.3%) were assigned to the intervention group, while 34 (50.7%) were in the control group. The highest frequency was observed in the 55- to 59-year-old age group, which accounted for 25.4%. The frequency for both the 60- to 64-year-old and 65- to 69-year-old age groups was identical, with eleven individuals in each group representing 16.4%. In the intervention group, there were 28 male patients (84.9%) and five female patients (15.1%). In the control group, there were 27 male patients (79.4%) and seven female patients (20.6%). Overall, the study included 55 male patients (82.1%) and 12 female patients (17.9%). The statistical significance of the differences in gender distribution between the groups was insignificant ($P = 0.601$).

The most common educational qualification among participants in the intervention and control groups was a diploma, with 29 participants (43.3%) holding this qualification ($P=0.99$). Of the study participants, sixty-three (94%) had undergone CABG surgery, while only four had valve surgery. Seventeen patients (25.4%) had a history of smoking; among them, 7 (21.2%) were in the intervention group, and 10 (29.4%) were in the control group ($P=0.484$). In the intervention group, 15 individuals (45.4%) had diabetes, while 16 individuals (47%) in the control group also had diabetes ($P=0.592$). Among the patients, three (9%) had a history of drug use, all of whom were in the intervention group ($P=0.224$). In a study examining the history of high blood pressure, 25 people (37.3%) were diagnosed with this condition. Among them, 13 patients (39.4%) were in the intervention group, while 12 patients (35.3%) were in the control group

($P=0.527$). In the intervention group, two patients (6%) and one patient (3%) in the control group had renal impairment. Overall, three patients (4.5%) experienced renal impairment ($P=0.608$).

There was no significant difference in MMSE scores between the two groups at 18-24 hours ($P=0.365$) and at 42-48 hours ($P=0.136$). However, the mean scores of the MMSE were lower after the intervention compared to before it ($P<0.05$) (Table 1).

Table 1. The mean of MMSE before and after intervention between the two groups

Items	Intervention	Control	P-value
Before	28.93±4.12	28.64±4.26	0.17
18-24 hours	26.5±4.26	25.55±4.64	0.365
42-48 hours	26.84±3.85	25.26±4.62	0.136

In the intervention group, 5 participants (16.1%) experienced delirium, compared to 13 participants (38.2%) in the control group ($P=0.057$). There was no significant association between the group and the occurrence of delirium (Table 2). There is a significant association between education level and the incidence of delirium in this study ($P = 0.003$).

Table 2. Examining the association of delirium by group

Items	Intervention	Control	P-value
Yes	5 (16.1%)	13 (38.2%)	0.057
No	26 (83.9%)	21 (61.8%)	

Discussion

Tests conducted to compare the MMSE scores 18 to 24 hours after surgery indicated no significant difference between the control and intervention groups. Additionally, there was no significant relationship between the MMSE scores in the control group at 18 to 24 hours after surgery and the MMSE scores in the intervention group at 42 to 48 hours after surgery. There was no significant relationship between the MMSE scores measured 42 to 48 hours after surgery in the control group and those measured 18 to 24 hours after surgery in the intervention group. Additionally, there was no significant relationship when comparing the MMSE scores 42 to 48 hours after surgery in the control group with those in the intervention group at the same time point. However, in the study by Bagheri et al. ¹⁶, a significant relationship was found when comparing the MMSE scores before and 48

hours after surgery in the intervention group, which aligns with our results.

Next, the relationship between the incidence of delirium in the intervention and control groups was analyzed by gender. In the control group, there was no significant relationship between individuals who developed delirium and individuals who did not have symptoms consistent with delirium in either male or female. In the intervention group, there was no significant relationship between male and female genders and the incidence of delirium, and overall, no significant relationship was found between the incidence of delirium and either male or female in this study. In the study by Zolfaghari et al. ¹⁷ and Bagheri et al. ¹⁶, there was no significant relationship between gender and the incidence of delirium, which is consistent with our study. In the study by Munk et al. ¹¹, there was a significant relationship between gender and the incidence of delirium, which is inconsistent with our study. The relationship between the incidences of delirium was evaluated by age, and in the control and intervention groups, there was no significant relationship between age and incidence. In the study of Iverd et al. ¹⁸, the study of Rudolph et al. ¹⁹, and the study of Bagheri et al. ¹⁶, there was a significant relationship between age and the incidence of delirium, which is inconsistent with our study.

In examining the relationship between the incidence of delirium in the intervention and control groups according to the level of education, there was an utterly significant relationship between the level of education and the incidence of delirium in this study. In the study of Iverd et al. ¹⁸, Rudolph et al. ¹⁹, and Randshagen et al., there was a significant relationship between education and the incidence of delirium, which is consistent with our study. In the study of Zolfaghari et al. ¹⁷, there was no relationship between education and the incidence of delirium, which is inconsistent with our study.

Conclusion

In this study, a total of 18 out of 67 patients developed delirium after heart surgery, which is a significant statistic. In the control group, 13 patients developed delirium after surgery, while in the intervention group, five patients experienced delirium. The analysis indicates a significant relationship between education levels and the occurrence of delirium. An important relationship has been observed between education and the occurrence of delirium, which aligns with our research findings. Some studies have used multimodal approaches, while others have tailored education to meet individual patient needs. However, the key takeaway is that education plays a

crucial role in reducing the incidence of delirium following heart surgery. It is essential to prioritize pre-surgery education, particularly in centers that perform heart surgery. All patients who are candidates for this type of surgery should receive comprehensive education, detailed planning, and a written program. Specific key hospital indicators, like the length of stay in the ICU and the overall hospital stay duration due to post-surgical delirium, can increase. These factors will impact the healthcare economy by raising costs for medical centers and placing additional financial burdens on insurance organizations.

Highlights

What Is Already Known?

Delirium is a sudden and temporary cognitive impairment that affects brain function.

What Does This Study Add?

Education decreased the incidence of delirium after cardiac surgery in the intervention group, while increasing age and higher education levels also contributed to a reduced incidence.

Authors' Contributions

Concepts, data gathering, data analysis, writing, and editing of the paper: Seyed Mohammadreza Amouzegar Zavareh, Mohammad Sadegh Pour Abbasi, Seyed Alireza Amouzegar Zavareh, Masoud Latifi-Pour

Acknowledgements

None.

Conflicts of Interest Disclosures

The authors declare that there is no conflict of interest.

Consent For Publication

The authors agree on publication.

Ethics approval

After receiving approval for the research, the code of ethics was obtained and registered with the Ethics Committee of Kashan University of Medical Sciences and Health Services under ID IR.KAUMS.MEDNT.REC.1400.133.

The extent of AI use

None

References

1. Danaee Fard H FA, Shool H, Shool S. Exploring antecedents of employees' soldiering in the public sector: A mix method research. *Organizational Behaviour Studies Quarterly*. 2017;5(4):1-20. [Doi:10.1001.1.23221518.1395.5.4.1.7](https://doi.org/10.1001.1.23221518.1395.5.4.1.7).
2. Mozafari M, Nejad S, Bagheri J, Peyvstegar M, Saghafinia M. Assessment of cognitive impairments following coronary artery bypass surgery with emphasis on working memory performance. *Tehran University Medical Journal*. 2020;78(3):165-70.
3. Weiser TG HA, Molina G, Lipsitz SR, Esquivel MM, Uribe-Leitz T, et al. Size and distribution of the global volume of surgery in 2012. *Bulletin of the World Health Organization*. 2016;94(3):201. [Doi:10.2471/BLT.15.159293](https://doi.org/10.2471/BLT.15.159293).
4. Benjamin EJ BM, Chiuve SE, Cushman M, Das SR, Deo R, et al. Heart disease and stroke statistics—2017 update: a report from the American Heart Association. *circulation*. 2017;135(10):e146-e603. [Doi:10.1161/CIR.0000000000000485](https://doi.org/10.1161/CIR.0000000000000485).
5. Ranjbaran S DT, Sadeghniaat-Haghighi K, Majdabadi MM. Poor sleep quality in patients after coronary artery bypass graft surgery: An intervention study using the PRECEDE-PROCEED model. *The Journal of Tehran University Heart Center*. 2015;10(1):1. PMID: PMC4494514
6. Bairami F, Ghorbanpoor M, Bairami A, Mostofian F. Assessment of patient safety friendly hospital initiative in three hospitals affiliated to Tehran University of medical sciences. *Journal of Patient Safety & Quality Improvement*. 2016 Jan 1;4(1):334-9. [Doi:10.22038/psj.2016.6312](https://doi.org/10.22038/psj.2016.6312).
7. Grover S, Ghosh A. Delirium tremens: assessment and management. *Journal of clinical and experimental hepatology*. 2018;8(4):460-70. [Doi:10.1016/j.jceh.2018.04.012](https://doi.org/10.1016/j.jceh.2018.04.012).
8. Gelinac C, Arbour C, Michaud C, Robar L, Côté J. Patients and ICU nurses' perspectives of non-pharmacological interventions for pain management. *Nursing in critical care*. 2013;18 (6):307-18. [Doi:10.1111/j.1478-5153.2012.00531.x](https://doi.org/10.1111/j.1478-5153.2012.00531.x).
9. Özer N, Özlü ZK, Arslan S, Günes N. Effect of music on postoperative pain and physiologic parameters of patients after open heart surgery. *Pain Management Nursing*. 2013;14(1):20-8. [Doi:10.1016/j.pmn.2010.05.002](https://doi.org/10.1016/j.pmn.2010.05.002).
10. Weiser T RS, Thompson K, Haynes A, SR Lipsitz others. An Estimation of the Global Volume of Surgery: A Modelling Strategy Based on Available Data" *The Lancet*. 2008;372(9633):139-44. [Doi:10.1016/S0140-6736\(08\)60878-8](https://doi.org/10.1016/S0140-6736(08)60878-8).
11. Monk TG WB, Garvan CW, Dede DE, Van Der Aa MT, Heilman KM, et al. Predictors of cognitive dysfunction after major noncardiac surgery. *The Journal of the American Society of Anesthesiologists*. 2008;108(1):18-30. [Doi:10.1097/01.anes.0000296071.19434.1e](https://doi.org/10.1097/01.anes.0000296071.19434.1e).
12. Wei LA, Fearing MA, Sternberg EJ, Inouye SK. The Confusion Assessment Method: a systematic review of current usage. *Journal of the American Geriatrics Society*. 2008;56(5):823-30. [Doi:10.1111/j.1532-5415.2008.01674.x](https://doi.org/10.1111/j.1532-5415.2008.01674.x).
13. Koster S, Hensens AG, Oosterveld FG, Wijma A, van der Palen J. The delirium observation screening scale recognizes delirium early after cardiac surgery. *European Journal of Cardiovascular Nursing*. 2009;8(8):309-14. [Doi:10.1016/j.ejcnurse.2009.02.006](https://doi.org/10.1016/j.ejcnurse.2009.02.006).
14. Devlin JW ,Fong JJ, Howard EP, Skrobik Y, McCoy N, Yasuda C, et al. Assessment of delirium in the intensive care unit: nursing practices and perceptions. *American Journal of Critical Care*. 2008;17(6):555-65. [Doi:10.4037/ajcc2008.17.6.555](https://doi.org/10.4037/ajcc2008.17.6.555).
15. Mandal S BM, Kirtania J, Sarbapalli D, Pal R, Kar S, et al. Impact of general versus epidural anesthesia on early post-operative cognitive dysfunction following hip and knee surgery. *J Emerg Trauma Shock*. 2011 Jan;4(1):23-8. [Doi:10.4103/0974-2700.76829](https://doi.org/10.4103/0974-2700.76829).
16. BAGHERI K, HONARMAND A, HOSSEINI MSJ. Association of mean arterial pressure during cardiopulmonary pump and incidence of delirium after coronary artery bypass graft surgery. 2017.
17. Mitra Z, Mohamad A, Shadan Pedram R, Khadijeh B, Ali B. Effectiveness of a multifactor educational intervention on delirium incidence and length of stay in patients with cardiac surgery. 2012.
18. Evered LA, Silbert BS. Postoperative cognitive dysfunction and noncardiac surgery. *Anesthesia & Analgesia*. 2018;127(2):496-505. [Doi:10.1213/ANE.0000000000003514](https://doi.org/10.1213/ANE.0000000000003514).
19. Rudolph JL, Schreiber KA, Culley DJ, McGlinchey RE, Crosby G, Levitsky S, et al. Measurement of post-operative cognitive dysfunction after cardiac surgery: a systematic review. *Acta Anaesthesiologica Scandinavica*. 2010;54(6):663-77. [Doi:10.1111/j.1399-6576.2010.02236.x](https://doi.org/10.1111/j.1399-6576.2010.02236.x).