Effect of environmental factors and gynecological interventions on quality of life during perimenopause

PhD thesis

by

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“Happiness is not a state but an activity.” (Aristotle)

1. INTRODUCTION

WHO defines Quality of Life as individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of their environment .(Bonomi, Patrick, Bushnell, & Martin, 2000).

Menopause is characterised by the cessation of cyclic ovarian function and a gradual decrease in hormone production of the ovaries, followed by the lack of menstruation. By definition, it is the state, when the last menstruation caused by cyclic change in ovarian hormon production is not followed by another on within 12 months (Soules et al., 2001).

The key step in menopause is in the ovary when the available primordial follicle pool for any further maturation process becomes empty. This affects the hypothalamo-hypophyseal system, resulting in elevated levels of gonadotropins in the blood stream. Sexual steroids are also produced in the reticular zone of the adrenal gland. In postmenopause, this mechanism is partially continued (F. Labrie, Luu-The, Labrie, & Simard, 2001), mainly contributing to further synthesis of estrogens in the fat tissue. Bilateral salpingo-oophorectomy in a fertile woman causes menopause-like changes, similarly to irradiation or chemotherapy affecting the ovaries.

Various symptoms of menopause are known, ranging from complete lack of symptoms to tremendous impairement of quality of life and shrinking of daily routine activities (Nelson, 2008). Symptoms can mostly be attributed to the change in endocrine functions (Guthrie, Dennerstein, Hopper, & Burger, 1996), but others may also be accounted (Pimenta, Leal, Maroco, & Ramos, 2012). It is supposed that, beside restoring hormonal functions, an optimal change in lifestyle factors is important in the alleviation of menopausal symptoms. Loss in bone mineral density is slowed by appropriately applied exercise, or the increase of daily intake of calcium along with Vitamin D3 (Heinonen et al., 1996; Ziegler, Scheidt-Nave, & Scharla, 1995). Certain natural ingredients in food, for instance flavonoids, may exert estrogen-like effect through estrogen receptors in the human body, thus providing possible platform for natural source to provide sufficient amount of estrogen when it is no longer produced by the physiological source organ

(Miksicek, 1994). Shifting dietary traditions toward these directions might be of future help in this regard.

2. AIM OF THE WORK

A. The onset of cardiovascular diseases, such as an acute myocardial infarction (AMI) shows certain circadian and seasonal variation. The development of vascular diseases may also be influenced by age and sex. We aimed to study the possible relations between the incidence of coronary heart attack (AMI) and age in females. Further, these investigations were extended to find possible seasonal or monthly variations in the incidence. We investigated if there is any difference in the incidence of coronary heart attack between premenopausal and postmenopausal women, in light of seasonality. The purpose of our study was to find out whether a weekly variation or a seasonal variation could be found in the occurrence of a heart attack in the group of women.

B. We also wanted to investigate if there is any impact of salpingectomy during hysterectomy, on the survival and function of the preserved ovaries. Systematically reviewing our patient databases covering 19 years back, we compared patients who underwent prior hysterectomy with or withouth salpingectomy, with special focus on the incidence of a second surgical intervention mandated by pelvic mass deriving from the adnexae. End points were the incidence of cystic degeneration of the ovaries and the appearance of that after hysterectomy. Based on our best knowledge, this has been the first study published in the international scientific literature dealing with the potential long term impact of salpingectomy at the time of hysterectomy on the survival of the ovarian function.

3. MATERIALS AND METHODS

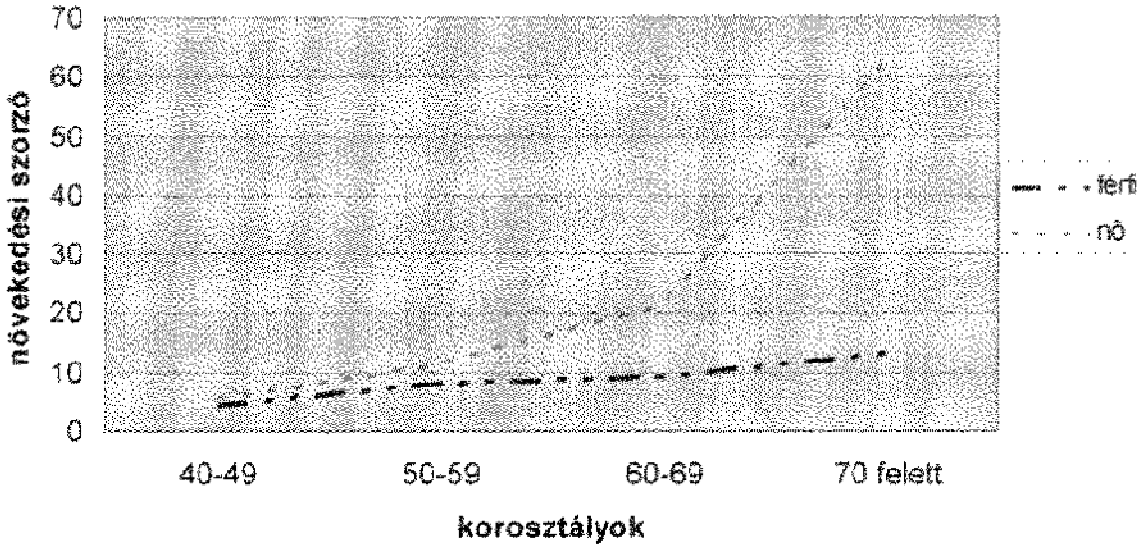
A. We have carried out a retrospective analysis among women with the diagnosis of AMI (n=32,345) admitted to hospitals between 2000 and 2004 in Hungary, grouped in age groups below and above the age of 50. Data was collected from the data base of the National Health Insurance Fund according to the International Classification of Diseases (ICD121,122). For statistical analysis, ANOVA, Kruskal–Wallis Test and Chi-square test were used and data were analyzed by SPSS 11.0 statistical software.

B. In a retrospective analysis covering a 19-year period, we collected data from 82 patients from our department who had previously undergone hysterectomy, and later on a second surgery due to an adnexal condition. A follow-up time of a minimum of 10 years was ensured. Patients were categorised with regard to the presence (Group I, n = 45) or absence (Group II, n = 37) of the Fallopian tube. The sample size was determined by the availability of patients for a long-term follow-up study. Further distinction was made based on the number of ovaries/adnexae preserved during the first operation. Only those patients with preserved tubes were included in the analysis, in whom no comment on any pathological alteration (e.g. tubal adhesions) of the Fallopian tube(s) had been made during the initial surgery. Also, we categorised further subgroups based on the type of the second surgery, focusing on their success rates. Since the cause of the initial surgery might later have an influence on developing hydrosalpinx in the group in which one or both tubes were preserved, we analysed data regarding the diagnoses prior to hysterectomy. Beyond that, specific data analysis included: the complaints; the age of the patient; the preservation of the Fallopian tube during the first surgery; the number of ovaries/adnexae left intact at hysterect- omy; the time interval between hysterectomy and the occurrence of adnexa-related complaints; diagnoses prior to first and second surgery; the type of the second surgery (laparoscopy vs. laparotomy); the histological diagnosis after second surgery; and the success rates of the second surgery obtained by interviewing patients at follow-up examinations. The underlying reasons for adnexa-related complaints were diagnosed based on clinical signs, and on physical and ultrasound examinations. For statistical analysis, the Kruskal–Wallis One-Way Analysis of Variance on Ranks and the Mann–Whitney Rank Sum Test were performed. Data were expressed as mean ± standard error (S.E.) and median values. Significance was determined by a ‘‘p’’ value equal to or lower than 0.05. For statistical analyses a licensed version of Sigma Stat for Windows (Systat Software Inc.) was used.

4. RESULTS

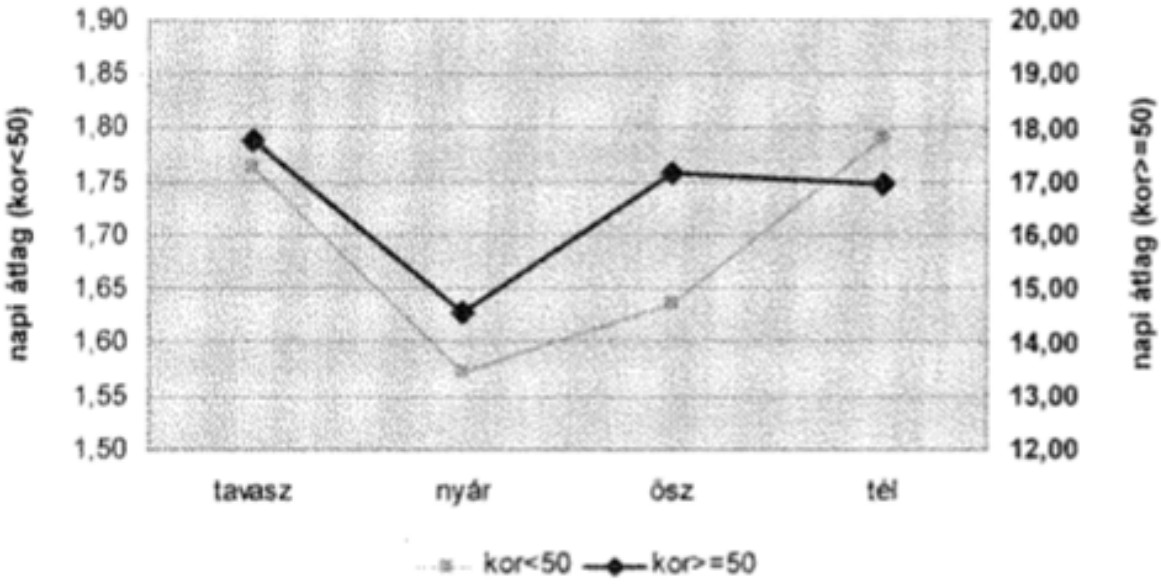
A./ AMI cases and seasonality.

Within the timeframe to be covered, data of 32,345 patients suffering AMI and admitted to hospital were analyzed. Number of female patients during the 5 years study period showed a significant, steady increase. Among female patients, a slow increase in case numbers above 55 years of age, while a sudden, marked increase above age 65 was noted, compared to those belonging to the age group below 40 years. On the other hand, among male patients, a slow but steady increase was observed from age 40 onward.



Increase in number of cases of acute myocardial infarction in comparison to subgroup of patients below 40 years of age between 2000-2004 in Hungary (n=72617)

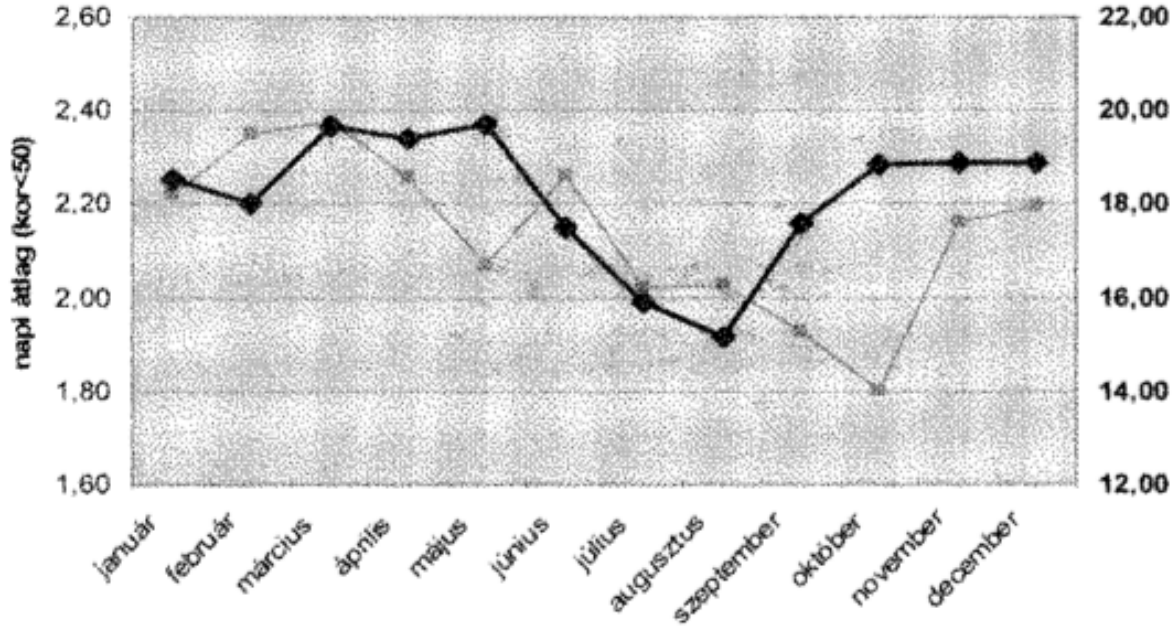
With consideration to seasonal variation, the peak period of AMI was during Spring, with the lowest number of events during Summer months.



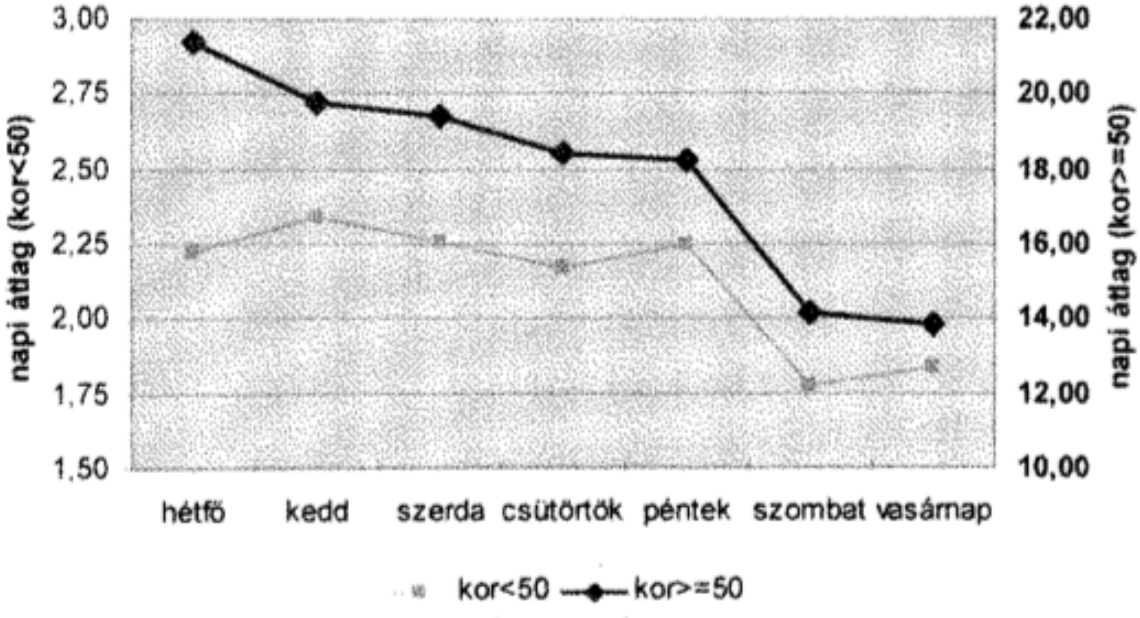
Seasonal distribution of AMI cases among women between 2000-2004 (n=32345)

There was significant difference between numbers of events in each season (p<0.0l). The weekly peak period of AMI morbidity was found on the first day of the week, Monday; showing a

gradually decreasing tendency until the last day of the week, Sunday ($p<0.01$). No significant difference was found between the two age-groups regarding seasonal or weekly variation.



Monthly distribution of AMI cases among women between 2000-2004 (n=32345)



Weekly distribution of AMI cases among women between 2000-2004 (n=32345)

B./ Survival and function of the preserved ovaries

Complaints in the two groups included lower abdominal pain, and pain during sexual intercourse or defecation. The diagnoses prior to hysterectomy for the two groups are shown in Table 1. In general, in Group I (Fallopian tube present), no hysterectomy was performed due to a pelvic

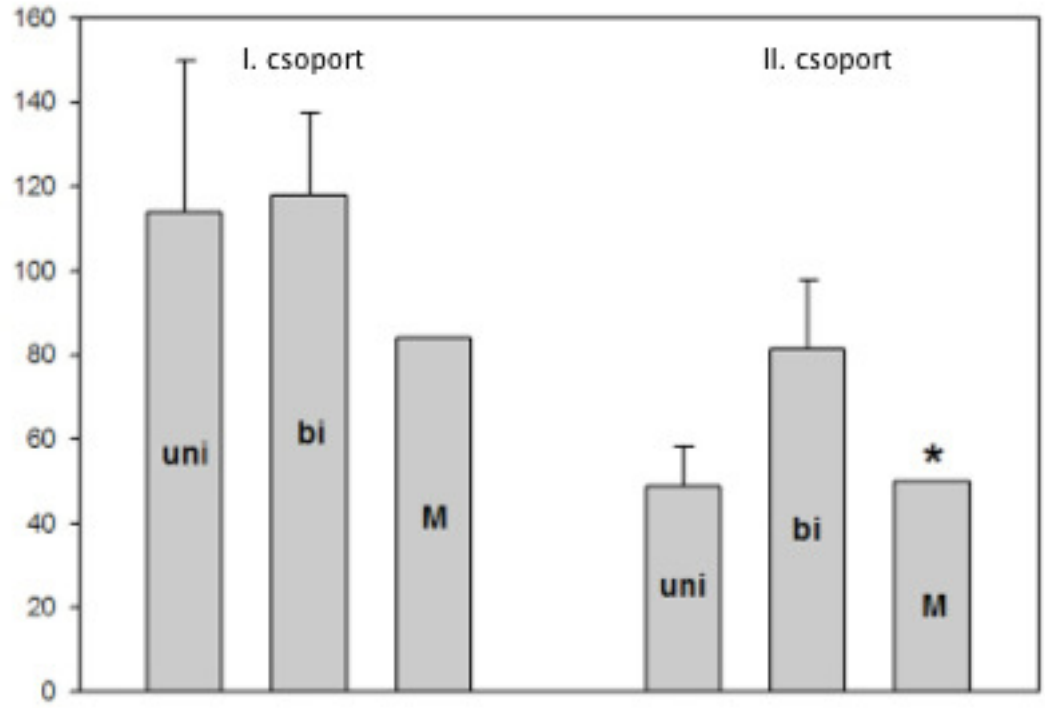
alteration that could subsequently increase the chance of developing hydrosalpinx (purulent pelvic inflammation, pelvic pain caused by extensive pelvic adhesions), except for endometriosis in two cases. In the endometriosis cases, however, the pelvic masses that developed later were ovarian cysts instead of hydrosalpinx. Fibroids and dysfunctional uterine bleeding together accounted for the indication for primary surgery in approximately 84% of cases in both Group I and Group II.

	Group I.	Group II.
Myoma	20 (44.4%)	24 (64.8%)
Endometriosis	2 (4.4%)	0
DUB	18 (40%)	7 (18.9%)
Cc.in situ	2 (4.4%)	1 (2.7%)
Prolapse	1 (2.2%)	0
PPH	1 (2.2%)	2 (5.4%)
PPID	0	2 (5.4%)
Benign ovarian tumor	0	1 (2.7%)
Endometrial atypia	1 (2.2%)	0

Diagnoses prior hysterectomy. DUB, dysfunctional uterine bleeding; PPH, post partum haemorrhage (including placenta praevia); PPID, purulent pelvic inflammatory disease

Group I (Fallopian tube present)

The number of patients in this group was 45, with a mean age of 50.8 years. Unilateral adnexa was found in 10 cases; in the remaining 35 cases bilateral adnexae were present. The time interval between hysterectomy and the occurrence of complaints was found to be 114.1 ± 35.9 and 117.9 ± 19.5 months in the uni- and bilateral adnexae subgroups, respectively (the differences between the subgroups were statistically non-significant).



*Elapsed time between hysterectomy and the occurence of symptoms caused by pelvic mass mandating second surgery in months (vertical axis). Group I.: Fallopian tube present; Group II.: Fallopian tube absent. Bars represent mean±standard error, uni: unilateral ovary/adnexa, bi: bilateral ovaries/adnexae. M: median value. * statistically significant where p=0,031.*

The median value for the time interval between first surgery and the onset of complaints in Group I was 84.2 months. The diagnosis prior to the second surgery was hydrosalpinx in 16 cases, which represents 35.5% of all cases. Other diagnoses were ovarian cyst or endometrioma in 28 (62.2%) cases or in one case (2.2%), respectively. All clinical diagnoses were then confirmed by histological examination. No malignant disease of the adnexae was found in this patient group. During the 19-year retrospective period, two cases of post-hysterectomy Fallopian tube neoplasm were found and the patients operated upon in our department.

Group II (Fallopian tube absent)

The number of patients in this group was 37, with a mean age of 46.7 years (there was no statistical difference between the two groups). Unilateral ovary was found in 15 cases; in the remaining 22 cases it was preserved bilaterally. The time interval between hysterectomy and the occurrence of complaints was found to be 48.6 ± 9.7 and 81.5 ± 16.3 months in the uni- and bilateral adnexae subgroups, respectively (the differences between the subgroups were statistically non-significant, Fig. 1). The median value for the time interval between first surgery and the onset of complaints in Group II was 50.0 months (p = 0.031, Fig. 1, Table 3). The diagnoses prior to the second surgery were ovarian cyst in 36 cases (97.2%) and neoplasm of the ovary in one (2.7%) case (Table 2), which were later confirmed by histological examination.

5. SUMMARY

It is clear that the number of AMI cases among women shows a slow increase above age 55 years and a marked increase above age 65 years, while that of men shows a slow but steady increase above age 40. This phenomenon among women can be attributed to the cessation of reproductive lifespan and the following characteristic changes in the endocrine and metabolic processes, and their negative impact on the cardiovascular system. The results of our study also suggest that AMI incidence in women shows a characteristic variation regarding seasons and the days of the week, which should be taken into consideration in the development of prophylaxis strategies.

Beyond environmental factors, medical activities involving surgical interventions affecting ovarian function might also play an important role in the onset of menopause. However, surgery that aims to preserve the nonfunctional Fallopian tube at the time of hysterectomy not only poses oncological risk to the patient, but it may serve as a ground for later complication in the form of a pelvic mass that mandates surgery again. On the other hand, careful manipulation is necessary during the removal of the Fallopian tubes when preserving the ovaries to avoid early cystic degeneration of the gonads and as a consequence, onset of menopause.

6. NEW RESULTS

1. Among female patients, a slow increase in case numbers above 55 years of age, while a sudden, marked increase above age 65 was noted, compared to those belonging to the age group below 40 years. On the other hand, among male patients, a slow but steady increase was observed from age 40 onward.
2. In Hungary, the peak period of AMI shows seasonal and weekly changes.
3. The peak period of AMI in Hungary was during Spring, with the lowest number of events during Summer months.
4. Risk of AMI is higher on workdays, especially early in the week, as compared to weekends.
5. Preserved Fallopian tube relatively frequently transforms into hydrosalpinx that mandates second surgical interventions following hysterectomy.
6. Time between hysterectomy and second surgical intervention because of a pelvic mass is significantly shorter among those with “orphan” ovary, highlighting the possibility of an impaired blood supply of the retained ovaries.
7. Success of a second surgery is independt of the type of the second surgery (laparoscopy vs. laparotomy).

7. ACKNOWLEDGEMENT

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8. LIST OF PUBLICATIONS

International publications:

1. Repasy I, Lendvai V, Koppan A, Bodis J, Koppan M. Effect of the removal of the Fallopian tube during hysterectomy on ovarian survival: the orphan ovary syndrome. Eur J Obstet Gynecol Reprod Biol. 2009 May;144(1):64-7. (IF: 1.582)
2. Garai J, Világi S, Répásy I, Koppán M, Bódis J. Short communication: seasonal onset of menopause? Hum Reprod. 2004 Jul;19(7):1666-7. (IF: 3.365)

Hungarian publications:

1. Garai J, Világi Sz, Répásy I, Bódis J. A menopausa-syndroma és környezeti tényezők. Egy kétdőíves pilot-tanulmány kezdeti tanulságai. Magyar Nőorvosok Lapja 61, 289-295 (1998).

2. Répásy I, Kriszbacher I, Vas B, Vas G, Bódis J. A szívinfarktus előfordulásának szezonalitása nőknél. Magyar Nőorvosok Lapja 70, 377-381 (2007)

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4. Répásy I, Kovács G, Koppán Á, Kriszbacher I, Bódis J, Koppán M. A petefészkek túlélése méheltávolítás kapcsán elvégzett salpingectomiát követően – az árva ovárium szindróma: Magyar Nőorvosok Lapja 73, 275-279 (2010)
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