Nutrition of burned patients

Daiva Gudavičienė, Rytis Rimdeika, Kęstutis Adamonis
Clinic of Surgery, 1Clinic of Gastroenterology, Kaunas University of Medicine Hospital, Lithuania

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Summary. Burns form 5–12% of all traumas. About 2,200 of patients are annually hospitalized in Lithuania. In most cases people of the employable age get burned. The treatment is often long-lasting, and afterwards recovered patients often have invalidity from burn sequels. The mortality of hospitalized burned patients is about 10%. The most common causes of death are pulmonary edema, pneumonia, sepsis and multiorgan failure. All these complications are related with insufficient nutrition. These complications are extremely frequent and dangerous for patients with more than 20% of body burned. The nutritional support of burned patient gives a possibility to increase the survival probability, to decrease complication rate and hospitalization time. Currently in Lithuania there are no standards for burned patient nutrition. More attention is given to strategy of surgical strategy and techniques, as well as antibiotic therapy. This article is the review of the different aspects of artificial nutrition of burned patient: indications, modes of nutrition, mixtures and terms of nutritional support.

Introduction
The assurance of the needs of nutritional factors and energy is essential for patients having more than 20% of the body surface (BS) burned. Such patients comprise a fair amount of people being treated in the Center of Burns of Kaunas University of Medicine Hospital (KUMH): in 1991–1998 patients having 21–30% BS burned comprised 19% of all treated patients, respectively 31–40% BS – 9.5% of patients, 41–50% BS – 3% of patients, 50% and over BS – 2% of patients (1). The mortality from burns in the Center of Burns of KUMH varied from 6 to 12% in 1973–1995 (1) and in 2000 it reached 18%. In 2000 there was a notably high number of patients having an especially heavy trauma from burn. The hospital treatment for burned patients is long. It varied from 47.97±43.09 days in 1981 to 30.85±22.77 days in 1991 and 26.6±19.52 in 2001 (2). We assume that it would be possible to avoid or modify live threatening complications, to save patients’ lives and reduce the hospital treatment time by assuring the complete nutrition. The aim of this article is to summarize the available experience concerning the nutrition of burned patients.

This topic is new in Lithuania. The standard of the nutrition of burned patients does not exist. By previous experience in our department up till now there was no routine administration of additional nutrition for burned patients. The most frequent choice was parenteral nutrition; therefore the infectious complications related to the central vein catheter were inevitable. This method of nutrition was being started to apply not right after the burn, but after the complications had begun. In this case the effectiveness of nutrition is limited. Currently in the Department of Plastic Surgery and Burns of KUMH the burned patients’ nutrition algorithm is established. We start the enteral nutrition in the early hours after the burn accident. In the process of developing the algorithm we could not implicitly follow the experience of rich West European countries as the conditions and possible facilities are different here. In France, for instance, burned patients are treated and dressed in isolated wards in order to avoid the transmission of the infection. While treating severe deep burns there is a possibility to cover the wound with artificial skin or keratocyte cultures. But in Lithuania it is still difficult to assure the medical care of burned patients in aseptic conditions. The majority of such patients are treated in 3 to 5 bed wards, dressed in special dressing wards, where the possibility of spreading hospital infection is high. While treating severe deep burns the problem of wound covering and donor spaces arise. Therefore the risk of infection is higher.
and the burns with more BS affected may be life threatening. Consequently, we must administer the enteral nutrition earlier than our colleagues in Western Europe do. Presently we think, that the enteral nutrition should be administered in a few hours after the burn for patients with >10% BS burned when the burn is of 3°, respectively 20% BS burned when a burn is 2B° and 30% BS when the burn is of 2A°. The prospective study currently being conducted in the Department of Plastic Surgery and Burns of KUMH will show if systemic enteral nutrition helps to reduce the amount of infectious complications, the hospital treatment time and if it makes the possibility to survive higher.

Energy requirements

According to H. Robert, the burn out of all traumas is the one, which causes the maximum disorder of metabolism. The energy requirements may increase with 100% (3). The reason is the secreted hormones and mediators released (4). Burns cause the major loss of energy and proteins. M. Belba states that it is possible to lose up to 40 g of nitrogen, 300 g of proteins, i. e. 1.5 kg of whole muscle mass. Such loss causes the vast demand for energy and nutrients. The required energy is produced by gluconeogenesis. The substratum here is vital amino acids and visceral proteins (5). J. Boucher made a research on metabolic changes of proteins in burns. In case of burn amino acids are converted to alanine, which disintegrates into pyruvates and they turn into glucose. Amino acids are wasted as gluconeogenesis is exceeding the demand of cells (6). Only a minor quantity of fat is used for producing energy while underfed; the major part is disassociated into fatty acids, which are resynthesized into fat because of the certain changes in hormone balance (7). Besides that the endogenic anabolic activity decreases because of burns. Therefore if a burned patient is not getting the proper nutrition, the visceral proteins are wasted, the muscle volume declines and as a result the organism is incapable to adapt to the existing situation and is not able to economize the use of energy (4). J. Manelli thoroughly described the changes in the immune system: the alteration of the corneous layer of epithelium “opens the gates” for the invasion of microorganisms. The wounds of a burn have perfect conditions for proliferation of microorganisms; therefore the immune state of a patient with burn is of crucial importance. However, the local and general defense mechanisms disarray while burned. The local resistance decreases because of death of Langhan’s cells or the disturbance of their function, decreased phagocytosis and chemotaxis by neutrophils and intracellular digestion of bacteria. Therefore insufficiency of cellular immunity develops. The general immune response weakens because of the influence of mediators – the activation of lymphocytes and synthesis of immunoglobulins is suppressed (7). The energy demands can be approximately determined using different metabolic formulas. Long’s modification of Harry–Benedict formula may be used for calculation of energy needs:

Male: $66.47 + (13.75 \times \text{weight in kg}) + (5 \times \text{height in cm}) - (6.76 \times \text{age in years}) \times AF \times BF$

Female: $65.51 + (9.56 \times \text{weight in kg}) + (1.85 \times \text{height in cm}) - (4.68 \times \text{age in years}) \times AF \times BF$

$AF$ – activity factor: cot-case – 1.2; walking – 1.3;
$BF$ – burn factor: deep burn – 2.1

However, obtained results are not definite as the burned area, its deepness, localization and possible presence of infection are not included in the formula (4). The Cuerry formula stays one of the most popular ones, it includes the area of BS:

Energy demand = 25 kcal/kg + 40 kcal/% BS area (4).

In spite of fact that demand of energy in patients with burns may reach 50 kcal/kg/d (4), it is important to keep the rational balance and do not overload the organism with huge amount of energy, which will not be assimilated. The study published in 2002 by D. W. Hart, emphasizes that 250 patients with burns of 10 to 99% of BS were examined. One of the groups was administered to get the proper amount of energy and the second – 1.2 times exceeded amount. Results showed that by administering higher amount than needed, the quantity of fatty tissue under the skin increased as the muscle volume did not change. D. W. Hart states that by exceeding the needed amount of energy, the number of complications increases and the mortality rate gets higher (8). In these later years administration of more than 30–40 kcal/kg per day is not recommended (4). Recent literature shows a tendency to decrease the loss and needs of energy by performing early necrotomies, keeping the right surrounding temperature, dressing with occlusal bandages, preventing or positively treating infections (4, 9, 10). The need for proteins per day is calculated according to this formula:

Protein need, g = 6.25 × (energy need, kcal) / 150.
Indications for enteral nutrition
Artificial nutrition after a burn is necessary when the needs of energy are not guaranteed with a routine nutrition. The majority of authors refer these indications for enteral nutrition:
1. More than 20% of BS is affected by burn;
2. Natural nutrition is impossible because of certain state of consciousness, face burn, injury of respiratory tract, artificial ventilation, tracheostomy.
3. The insufficient nutrition before the injury or the developing of such in a hospital, severe chronic diseases (4, 9).

Certain attention must be paid to patients having higher risk to multiorganic insufficiency. Those groups were excluded in a prospective study of 700 patients conducted by Y. Yonov. It is statistically significant that a higher risk to develop a multiorganic insufficiency exists for males of the age less than 50 and for females more than 50 years, when the respiratory tract is affected by burn, when the burned area exceeds 30% BS, the deep burn exceeds 10% of BS, sepsis or pneumonia are present (11). Because the digestive tract of burned patient is functional, the enteral nutrition is recommended (4, 10). The enteral nutrition is better than parenteral as it protects the intestinal mucous membrane, prevents bacterial translocation; is more physiological, the risk of infection is lower, and it is less expensive (4, 9, 12).

The contraindications for enteral nutrition in burned patients practically do not exist.

It is very important to start enteral nutrition in the first hours after burn (4, 9, 12). M. G. Jenchke was investigating groups of rats – with burns and undernutrition; he was studying impact of those two factors for the mucous membrane of their digestive tract. The results are: burn and undernutrition raised the number of enterocyte apoptosis, however the impact for the intestinal mucous membrane did not accumulate. The activity of mucous membrane proliferation was the same in both groups. Supposedly, an early enteral nutrition helps to keep the integrity of an intestinal mucous membrane (13). The study of J. Chen published in 1997 analyzed rats with 30% of the BS burned. It found, that the composition of bacteria is different after a burn – the number of anaerobes is lower, the number of Enterobacter and Candida is higher, the amount of IgA in caecum is diminished an endotoxemia in v. cava inferior is increased. In groups with Bifidum present in nutrition the amount of IgA in caecum increased and the rates of bacterial translocation and endotoxemia were lower comparing with the group without Bifidum. This suggests that administering Bifidum bacteria per os may lower bacterial and endotoxic translocation from the intestinal tract (14). However, these studies have not been conducted with people yet.

Enteral versus parenteral nutrition
A lot of studies with animals and people were conducted in order to determine, which method of nutrition is better – enteral or parenteral. The study of X. Peng, published in 2000, analyzed rats with 30% of the BS burned. Three groups were researched – enteral nutrition, parenteral nutrition and control one. The lesions of mucous membrane of digestive tract were less in the group with enteral nutrition (15). The study of L. X. Cui, conducted in the year 2000, showed that the amount of alpha tumor necrotic factor and mortality rate were much higher in the group with total parenteral nutrition comparing to one with enteral nutrition and the control one (16).

Methods of delivering enteral nutrition
Administration with nasogastric tube is recommended as this method is agreed to be the most physiological one. If wishing to administer the vast amounts of enteral mixtures, it may be done by nasoduodenal or nasojejunal tubes (4). The alternative, especially when planning a long-term nutrition, is a percutaneous gastrostome. In a retrospective study conducted in Netherlands by B. E. Kreis, two groups were compared – the first one received nutrition through nasogastric tube and the second one – through a percutaneous endoscopic gastrostome. Patients of the second group did not have any contraindications for nutrition, there were less complications and the discomfort of patients was lower. Performing the nutrition through percutaneous endoscopic gastrostome lessens the risk of regurgitation and aspiration (17). The meaning of percutaneous endoscopic gastrostome is without doubt important for patients having large BS burned or respiratory tract burned. In 1999 R. Sheridar wrote, that percutaneous endoscopic gastrostomies were performed for 14 patients with burns. Patients estimated this method of nutrition as a comfortable, there were only a small number of complications. Gastrostome was held for approximately 155 days (18).

Early versus late enteral nutrition
It was stated earlier that enteral feeding of the burned patient should be started only after the period of shock was over – i. e. the second or even the third day after the burn. Recently there are more supporters of an early enteral nutrition – it must be started in 6 hours after the burn. First studies showing advantages of a
early nutrition were conducted in 1994. L. Gianotti has proved, that early enteral nutrition lessens the translocation of bacteria (19). Data concerning the impact of an early enteral nutrition to catabolism is controversial. The study published in 1997 by S. Wang proved, that early enteral nutrition lessens catabolism after burn: the need of energy by burned patients was studied, as well as plasma glucagons, serum insulin, urine cortisol and catecholamines. Decrease of those indexes has been proven to be statistically reliable in the group with an early enteral nutrition comparing to the later enteral nutrition one (20). Though the study announced by J. Noodrenbos claimed that early necrectomy, coverage of wounds and aggressive early nutrition with mixtures rich in proteins did not inhibit distinct catabolism, that was characteristic for burns (21). There are different data about time interval, during which the enteral nutrition should be started. T. Raff affirms that if time interval from burn till beginning of nutrition is longer than 18 hours, treatment is more often unsuccessful; mortality does not decrease (21). Study announced in 2000 by J. L. Pereira also proves that beginning of nutrition is very important. This study investigated the influence of enteral nutrition to the frequency of development of septic syndrome. A retrospective research was conducted, 64 patients with more than 20% of BS burned were analyzed. In the first group 23 patients were included; nutrition was started under 24 hours after burn. In the second group of 41 patients nutrition was started later than 24 hours after burn. Statistically significant difference showed the advantage of early enteral nutrition – sepsis was diagnosed for 26% of first group patients and 54% of second group patients (23).

It is recommended to start enteral nutrition with hypo-caloric mixture (0.5 kcal/ml) in the rate of 25 ml per hour. If nutrition is well tolerated by patient, the rate is increased up by 25 ml every 8 hours, to 100–120 ml per hour (4).

**Contraindications for enteral nutrition**

Contraindications for enteral nutrition in burned patients practically does not exist; there are only few very rare common contraindications for enteral nutrition:
1. Disordered function of bowels due to inflammation, stasis.
2. There are no technical possibilities to probe.
3. Ethical aspects – terminal condition.

**Parenteral nutrition**

Parenteral nutrition can be ordered as addition to enteral nutrition when enteral nutrition is not sufficient, if central intravenous catheter is used for another purpose or if a patient does not tolerate enteral nutrition (10).

**Enteral nutrition mixtures**

Patients with burns should be given mixtures high in calories and proteins. Carbohydrates must be the main source of energy and must ensure 60–65% of energy required. Although this amount should not exceed the oxidation limits of the body, carbohydrates should be given not more than 5–7 mg/kg/min. It is necessary to measure glycemia and urine for glycosuria, as excess of carbohydrates is transformed to fat. It is recommended to provide 23–25% of energy given with proteins. High level of proteins overloads kidneys, so it is necessary to observe the balance of liquid, level of nitrogen and creatinine in blood. Fat must make around 40% of non-protein calories or 5–15% of all energy required. If lipid emulsions are given, it is necessary to observe the level of plasma triglyceride: it should be analyzed not earlier than 4 hours after completing lipid infusion and should not be exceeded (4). Because of special metabolism after burns, low-fat mixtures are recommended. A study conducted by D. R. Garel, investigated patients with burns, who were nourished with mixtures containing usual amount of fat (fat makes 35% of calories), with mixtures containing lower amount of fat (15% of calories) and with mixtures that were low in fat and contained cod-liver oil. In the group of mixtures with lower fat level after 30 days of nutrition number of cases of pneumonia was statistically significantly lower; better condition of respiratory and digestive systems, and shorter recovery time were observed (1.2 and 1.8 d/% of the body surface burned).

**Micronutrients**

Cod-liver oil didn’t increase the clinical efficiency of mixture with low fat level (24). A special attention in nourishing a burned patient should be paid to micronutrients that are lost through wounds, with urine and sequestering tissues (25). Some micronutrients like zinc, cooper and selenium are vital for healing of wounds and for normal function of immune cells. M. M. Berger ordered these microelements in doses 4–6 times higher than usual – there was a decrease in frequency of infectious complications and hospitalization time got shorter (26). The importance of vitamins is also recognized: vitamin C participates in immune response, acts like an antioxidant. B1, B6, B12 are important for wound healing. Vitamin E is an antioxidant. Vitamin A protects from stress caused ulcers (4).
**Immunomodulators**

The importance of some specific nutrients in burns is proved; these substances get a special attention in recent years. They are called immunomodulators. It is determined, that these substances have a positive affect on protein metabolism, immune state and function of intestines. The idea to administer branchy amino acids for burned patients came up when it was noticed that when there is an increased concentration of leucine in vitro the synthesis of muscle protein becomes more active, while proteolysis is inhibited (27, 28). E. Mori performed investigations with rats and concluded that imposition of branchy amino acids stimulated synthesis of muscle and liver protein (29). Data of human research are opposite. J. G. Manelli study shows that imposition of branchy amino acids decreases muscle proteolysis (it was proved while investigating 3-metilhistidine in urine) without influence on nitrogen balance (30). However, in Y. M. Yu study announced in 1988 the separating effect of branchy amino acids was not remarked (31). In recent years many studies on effect of immunomodulators – glutamine and arginine – were conducted. It is proved that after a burn there is a distinct decrease of glutamine in body (32), although glutamine synthesis gets more intensive de novo especially in muscles (33). Glutamine has many pharmacological effects. In experimental study by P. Furst it was proved that keeping a nourishment rich in glutamine in catabolic conditions gives a positive effect on nitrogen balance, protein synthesis, decreases proteolysis in muscles, helps to retain integrity of digestive tract, protects from translocation of bacteria, decreases the number of complications, as well as mortality and hospitalization time (34). The study of Y. Zhou announced in 1999 determined, that ordering of glutamine in early stage after burn in doses of 0.5–1 g/d decreased the risk of complications, improved wound healing and shortened hospitalization time (35). Another immunomodulator arginine is also known as a substance effecting metabolism and immunity. Effect of arginine is connected to its effect on nitrogen monoxide radicals and aliphatic groups of polyamines. C. Chntraskul claims that after a burn the need of arginine significantly increases, synthesis is no more able to satisfy needs (36). Data about ordering immunomodulators is also controversial. There are studies proving advantage of immune formulas. C. Chntraskul in 1998 ordered a diet rich in glutamine and omega-3 fatty acids and obtained a significant improvement of immune parameters and parameters, reflecting nutrition status (36). However a study by J. R. Saffle in 1997 didn’t show advantage of immune formulas against regular mixtures (37). It is appointed that ornithine alfa-ketoglutarate decreases catabolism of muscle and myofibril proteins, saves glutamine in muscle, decreases catabolism in intestine and stimulates protein synthesis in liver after burn (38). The effect of alfa-ketoglutarate for a burned patient is specific and complex; it depends on glutamine reserves. L. Cynober recommends administering alfa-ketoglutarate 2 times per day, altogether 10 g (2 bolus every 12 hours) (39). Omega-3 fatty acids (FA) have anti-inflammatory effect; they inhibit interaction of blood-vessels endothelium with leucocytes, inhibit synthesis of interleukines-1 and -6. Ratio of omega-6 FA and general FA level is important because synthesis of prostaglandins or leukotrienes predominates depending on this rate. It seems that not a high ratio of omega-6 and omega-3 causes immunosuppression (4, 40). After burns mixtures of immunomodulators can be used: glutamine, arginine, alfa-ketoglutarate, omega-3 fatty acids, selenium, zinc – cocktails. They can be used as stable mixtures for enteral nutrition (4, 40). Several studies analyzed effect of mixtures of immunomodulators for burned patients: J. R. Saffle’s study had an aim to create a mixture of immunomodulators for a routine use. Mixture enriched with arginine, branchy amino acids, omega-3 FA was used. Forty-nine patients were examined; no difference among morbidity and mortality, artificial lung ventilation and hospitalization length was noticed compared with control group (41). M.M. Gottschlich compared three groups: one group was given immunomodulating mixtures (omega-3 FA, arginine, cysteine, vitamin A, zinc, selenium, chromium), and two groups were nourished with standard enteral nutrition mixtures. In the group of immunomodulating mixtures there were less cases of skin infections, and hospitalization time was shorter (42).

**Monitoring of nutritional support**

It is very important to evaluate the efficiency of given nourishment, for consequence of insufficient nutrition is slower and malqualitative wound healing. Evaluation of nutritional state of burned patient should be started from clinical analysis. First sign of insufficient nutrition is fatigue of patient, while performing everyday procedures, as well as during kinesitherapy (43). Tolerance to enteral nutrition should be constantly observed as well; remaining volume of stomach should be measured and intestine transit should be observed. Routine laboratory analysis should be carried out: glycemia, balance of electrolytes, measures of kidney and liver function, and measures of protein metabolism. Anthropometrics measures: weight, Body Mass Index (BMI= kg/m²), upper arm size – do not make sense in...
initial phase after burn because of massive infusion therapy and changed distribution of liquids in interstitial tissue. Although absolute means of these measurements are not precise, they have to be done periodically, and measured in dynamics (4, 10, 43). If there is no insufficiency of kidney function, nitrogen balance is a good indicator of nutrition state and efficiency. Nitrogen balance is a difference between obtained and lost nitrogen (N). In practice secreted nitrogen is measured only in urine, but it is necessary to specify nitrogen loss while including other physiological ways of secreting nitrogen – with excrement, hair through skin – in exudation way (10).

Nitrogen loss = N is lost with urine + 8 mg/kg of weight + 0.2 g N/% BS burned.

This formula can be used only first ten days after burn. On the basis of laws of physiology, from 80 to 85% of urine nitrogen makes urea. That is why we can easily count the level of nitrogen secreted with urine if we know the level of urine urea:

\[ N_{\text{urine}} = \left( \frac{\text{urea in urine} \times 0.08}{2.14} \right) + 4 \text{ g} \]

Here 0.08 is a coefficient to convert urea from g/l into mmol/l; 2.14 is a coefficient of recalculation used to find out the level of nitrogen in urine form urea level in urine; 4 g is not N of urea (ammonia, creatinine, urine acid, free amino acids, etc.) (44). These calculations are pretty precise for patients with burns of an average extent. But they can be erroneous in case of burns of more than 50% of the body surface or sepsis. In such case loss of nitrogen is evaluated insufficiently, for such patients have a turn for acidosis; in such case production of nitrogen predominates, and it is not reflected in this formula. Therefore it is recommended to measure nitrogen level in urine directly (44). Proteins, nutrition state markers, are measured for evaluation of nutrition. Albumin (ALB), transthyretin (TTR, previously known as prealbumin) and retinol connecting protein (RBP) are good nutrition state markers in cases of acute nutritional disorders. After burn cytokines are secreted intensively and inhibit protein synthesis in liver. During first ten days after burn it is difficult to evaluate if these protein level changes are stimulated by change of nutritional state or inflammatory process. Inflammation markers (CRB) change should be taken into consideration while evaluating these changes. It is recommended to evaluate prealbumin every three days till 21st day after burn, later – once a week. In practice these proteins and their dynamics are excellent prognostic indicators of morbidity (healing deceleration, infection of wounds) and mortality (45, 46). Among these proteins prealbumin is the most suitable indicator of nutrition, because a half period of albumin dissociation is long and the feature to distribute in different tissue sectors after burn is known. Retinol connecting protein is more sensitive to kidney function disorders and detection of its level and is more expensive than TTR (45).

Discussion

Doctors healing burns were the first ones to introduce clinical nutrition in practice, for nutrition state is directly connected with prognosis and perspectives of burned patient.

At present early enteral nutrition is started in acute period of burn. Parenteral nutrition is used only in case of patient intolerance to enteral nutrition or in case it is insufficient.

The most popular questions in nutrition of burned patient are enteral versus parenteral nutrition, early versus late enteral nutrition, dose and composition of enteral nutrition (protein, carbohydrates, lipids, and immune-enhancing additives), strategies to optimize delivery of EN and minimize risks (motility agents, small bowel versus gastric feedings, elevation of the head of the bed, probiotics, and bolus administration) and enteral nutrition in combination with supplemental parenteral nutrition.

There are insufficient data to generate recommendations in the following areas: use of indirect calorimetry; optimal pH of enteral nutrition, supplementation with trace elements, antioxidants, or fiber; optimal mix of fats and carbohydrates; continuous versus bolus feedings; use of probiotics.

Scientific progress in field of nutrition is rather slow, because there are very few burn centers and therefore cohort studies are not possible. Alternative for cohort studies are multicentral studies. But in case of multicentral studies it is very hard to differentiate if obtained differences are due to different treatment tactics in different burn centers or due to nutrition. It is difficult to form homogenized groups due to the individual response to burn. In case of the same kind of burn the need of energy can differ up to 30% (46). Recently genes, determining response to stress, aggression, were discovered. So it might be possible to homogenize analyzed groups according to genetic aspects. However, today we could conclude that rather clear recommendations for nutrition of burned patients are found in literature, at least much more clear that some years ago.
Conclusions
When considering nutrition support in burned patients, enteral nutrition is strongly recommended to be used in preference to parenteral nutrition. The use of a standard, polymeric enteral formula that is initiated within 24 to 48 hours after admission is recommended. Strategies to optimize delivery of enteral nutrition (starting at the target rate, use of a feeding protocol using a higher threshold of gastric residuals volumes, use of motility agents, and use of small bowel feeding) should be considered. A glutamine-enriched formula should be considered for patients with severe burns and trauma. When parenteral nutrition is used, supplementing with glutamine, where available, is strongly recommended.

Nudegusių pacientų maitinimas

Daiva Gudavičienė, Rytis Rimdeika, Kęstutis Adamonis
Kauno medicinos universiteto klinikų Chirurgijos klinika, Gastroenterologijos klinika


Adresas susirašinėjimui: D. Gudavičienė, KMUK Chirurgijos klinika, El. paštas: daikle@centras.lt

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