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Fasting time and metabolic changes in elective surgeries: an integrative review

Tempo de jejum e alterações metabólicas em cirurgias eletivas: revisão integrativa
Tiempo de ayuno y cambios metabólicos en cirugías electivas: revisión integradora

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ABSTRACT
Objective: To identify in the scientific production the occurrence of metabolic changes in the postoperative period of elective surgeries and their relation with preoperative fasting time. **Method**: An integrative review carried out from June to July 2020 in the LILACS, MEDLINE, CINAHL, COCHRANE, SCOPUS, and EMBASE databases. Articles from 2015 to 2020 were selected. For the analysis of the evidence levels, the Oxford Centre for Evidence-Based Medicine categorization was followed. **Results**: A total of 10 scientific articles were selected. The metabolic changes found were hyperglycemia, elevated serum levels of IL-6, cortisol, and valine, increased insulin resistance, decreased glutamic acid plasma levels, and increased IGF-1 levels with a reduction of IGFBP-3. Shortening the fasting time minimizes the patient's organic stress, with a reduction of metabolic changes, hospitalization time and morbidity. **Conclusion**: Preoperative fasting time longer than eight hours is related to metabolic changes in the postoperative period. Major surgeries present the greatest metabolic changes.
KEYWORDS: Fasting; Metabolism; Elective Surgical Procedures; Patients.

RESUMO
Objetivo: Identificar na produção científica a ocorrência de alterações metabólicas no pós-operatório de cirurgias eletivas e sua relação com o tempo de jejum no pré-operatório. **Método**: Revisão integrativa, realizada de junho a julho de 2020 nas bases de dados LILACS, MEDLINE, CINAHL, COCHRANE, SCOPUS e EMBASE. Foram selecionados artigos de 2015 a 2020. Para a análise dos níveis de evidência seguiu-se a categorização de Oxford Centre for Evidence-Based Medicine. **Resultados**: Foram selecionados 10 artigos científicos. As alterações metabólicas encontradas foram hiperglicemia, elevação dos níveis séricos de IL-6, cortisol e valina, aumento da resistência insulínica, queda dos níveis plasmáticos de ácido glutâmico e elevação dos níveis de IGF-1 com a redução de IGFBP-3. A abreviação do tempo de jejum minimiza o estresse orgânico ao paciente, com a redução das alterações metabólicas, tempo de internação e morbidade. **Conclusão**: O tempo de jejum pré-operatório superior a oito horas está relacionado a ocorrência de alterações metabólicas no pós-operatório. As cirurgias de grande porte apresentam as maiores alterações metabólicas.
DESCRITORES: Jejum; Metabolismo; Procedimentos Cirúrgicos Eletivos; Pacientes.

RESUMEN
Objetivo: Identificar en la producción científica la existencia de cambios metabólicos en el postoperatorio de cirugías electivas y su relación con el tiempo de ayuno en el período preoperatorio. **Método**: Revisión integradora, realizada de junio a julio de 2020 de las bases de datos LILACS, MEDLINE, CINAHL, COCHRANE, SCOPUS y EMBASE. Se seleccionaron artículos de 2015 a 2020. Para el análisis de los niveles de evidencia se siguió la categorización del Oxford Center for Evidence-Based Medicine. **Resultados**: Se seleccionaron 10 artículos científicos. Las alteraciones metabólicas encontradas fueron hiperglucemia, niveles séricos elevados de IL-6, cortisol y valina, aumento de la resistencia a la insulina, reducción de los niveles plasmáticos de ácido glutámico y aumento de los niveles de IGF-1 con disminución de IGFBP-3. La disminución del tiempo de ayuno minimiza el estrés orgánico del paciente, con una reducción de los cambios metabólicos, la duración de la estancia hospitalaria y la morbilidad. **Conclusión**: Existe una relación entre un tiempo de ayuno preoperatorio mayor a ocho horas y la presencia de cambios metabólicos en el postoperatorio. Las cirugías mayores muestran los mayores cambios metabólicos.
DESCRIPTORES: Ayuno; Metabolismo; Procedimientos Quirúrgicos Electivos; Pacientes.

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INTRODUCTION

Preoperative fasting, required for carrying out surgical procedures, has been widely discussed in the last few years. In general, the traditional fasting practice corresponds to a period between eight and twelve hours of complete liquid and food restriction, and it can exceed twelve hours due to delays in the surgical schedule, cancellation of surgeries, or other factors(1).

An extended preoperative fasting period can promote sensations of thirst, anxiety and headache, which can negatively interfere with the postoperative period. In addition to that, extended fasting leads to metabolic stress triggered by the surgical trauma, generating an increase in insulin resistance and the occurrence of catabolic reactions in the organism, culminating in a longer hospitalization period and higher levels of postoperative complications(1).

Currently, new multi-professional and institutional protocols and guidelines have indicated the reduction of the traditional fasting practice as a strategy to accelerate postoperative recovery, based on the principles of the evidence-based practice(2). In 2001, the Enhanced Recovery After Surgery (ERAS), a European program on postoperative care, established a safe protocol with preoperative measures to optimize the nutritional aspects and implement carbohydrate-rich solutions in the preoperative period(2).

In Brazil, the Accelerated Total Postoperative Recovery (*Aceleração da Recuperação Total Pós-Operatória*, ACERTO) project was instituted. Created in 2005, the project suggests offering a maltodextrin solution up to two hours before the surgical procedure(3). Guidelines such as those set up by the European Society of Anaesthesiology (ESA) recommend solid food restriction to start between six and eight hours before anesthetic induction(4).

Shortening fasting time by the intake/administration of a carbohydrate-rich solution up to two hours before the surgery, as well as early feeding in the postoperative period, provides the patient with greater comfort and can optimize the reestablishment of the physiological functions, promoting a rapid restoration of the bowel functions, better glycemic control, and a reduction of surgical site infections in the postoperative period. However, the implementation of protocols aimed at this behavior still faces resistance in the assistance practice(2).

This research is justified as it supports the systematization and redirection of safe and quality assistance, as well as it leads the design of protocols aimed at patient safety and at the consolidation of new preoperative conducts, consequently improving the quality of the assistance provided to the surgical patient. Thus, this study has as its objective to identify in the scientific production the occurrence of metabolic changes in the postoperative period of elective surgeries and their relation with the fasting time in the preoperative period.

METHOD

This is an integrative review. Six stages were followed[5] to elaborate this study. To guide the formulation of the research question, carried out in the first stage of the study, the PICo strategy was used, a methodology employed to elaborate the question for evidence search in the literature, intended to non-clinical studies, as it is the case of this study. Thus, the research question was structured in three elements[6]: P (Patients); I (Fasting) and (Metabolism); Co (Elective Surgical Procedures). The following question was considered as the study question: "What are the metabolic changes that occur in the postoperative period of elective surgeries and their relation with the preoperative fasting time?"

In the second stage, the following inclusion criteria were determined: studies in adults over 18 years old, which address the issue of metabolic changes related to extended preoperative fasting in elective surgeries; methodological-based studies of experimental or quasi-experimental design; and time-series or control cases, indexed in the databases. As filters, "articles published in English, Spanish or Portuguese, produced in the last five years (2015-2020)" were used, seeking the most updated evidence on the theme. Articles with no clear method outlining, theses and dissertations, and articles not available in full for consultation were excluded, as well as protocols, Guidelines, and secondary-source studies. In the case of duplicate articles, only one copy was used.

The eligibility criteria were applied in the abstracts. The selection of the articles was initially carried out by a previous reading of the abstract, in order to verify its relation with the topic, so that full reading could be initiated. The search was carried out in the following databases: Latin American and Caribbean Literature in Health Sciences (*Literatura Latino-Americano e do Caribe em Ciências da Saúde*, LILACS) via the Virtual Health Library (*Biblioteca Virtual em Saúde*, BVS), International Literature in Health Sciences (MEDLINE) via PUBMED, SciVerse Scopus (SCOPUS), Cumulative Index to Nursing and Allied Health Literature (CINAHL) via CAFe, Cochrane Library (COCHRANE) via CAFe, and Excerpta Medica Database (EMBASE) via CAFe.

The following DeCS/MESH/Emtree thesaurus were used for the study: *Pacientes*/Patients/Patient, *Jejum*/Fasting, *Metabolismo*/Metabolism and *Procedimentos cirúrgicos eletivos*/Elective Surgical

Procedures/Elective Surgery. The definition of controlled descriptors was referenced under the Health Sciences Descriptors in Health Sciences (*Descritores em Ciências da Saúde*, DeCS) and Medical Subject Headings (MESH) terms.

Due to the specific features of each database, the search strategies were adapted according to the objective and inclusion criteria of this study. The search for the articles took place from June to July 2020.

Initially, isolated descriptors were used to search for the articles with the aid of the Boolean operator *OR*; however, a high number was obtained for the objective of this study. To enhance the search, the Boolean operator *AND* was included, in addition to *OR,* along with the association of four descriptors.

In the third stage, the full texts were evaluated by two reviewers regarding their methodological validity. The studies were classified in relation to the evidence level, according to the Oxford Centre for Evidence-Based Medicine[7] categorization, classified as 1A (systematic review), 1B (randomized clinical trial), 2A (systematic review of cohort studies), 2B (cohort study and randomized clinical trial of lower quality), 2C (research results), 3A (systematic review of case-control study), 3B (case-control study), 4 (case report), and 5 (specialist opinion and non-systematic review).

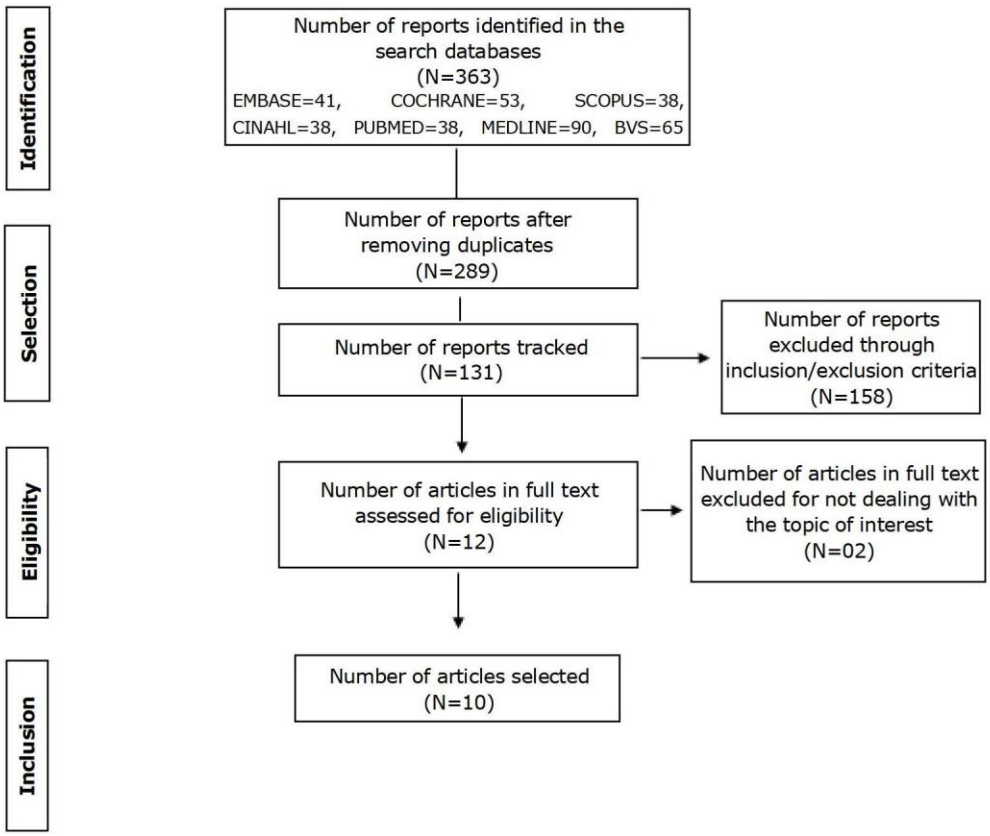
In the fourth stage, the selected texts were read and interpreted by completing an instrument previously elaborated by the author to obtain the information needed to analyze the metabolic changes in the postoperative period of patients subjected to extended preoperative fasting. For each primary study included, a synthesis chart was elaborated containing the following information: author(s), year of publication, type of study, level of evidence, objective(s) and main results.

To reduce the number of interpretation errors of the results and outlining of the analyzed studies (bias), the search was carried independently by evaluators in the same databases and with the same descriptors, in the end presenting 100% agreement in the findings. In addition to that, two reviewers verified the validation of the methodological quality in an independent manner. There was no disagreement between them.

RESULTS

A total of 10 articles that met the inclusion criteria previously established were analyzed for this integrative review. The selection process of the articles was described through a flowchart, as recommended in the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA)[8], which can be seen in Figure 1.

Figure 1: PRISMA flowchart (adapted) to the study selection and inclusion process. Rio de Janeiro, RJ, Brazil, 2020.



Regarding the databases, four articles (40%) were identified in PubMed and two (20%) were simultaneously found in EMBASE, Scopus, and the BVS. As for the year of publication, 40% (four articles) date from 2019. Among the articles analyzed, only one (10%) was developed in Brazil. The others correspond to international publication articles, as shown in Figure 2, with the features of the selected studies.

Figure 2: Summary of the selected articles. Rio de Janeiro, RJ, Brazil, 2020.

Author/Year/Country	**Type of study**	**Evidence Level** (Oxford Centre for Evidence-Based Medicine)	**Objective**	**Main findings**
Pędziwiatr M, Pisarska M, Matłok M, Major P, Kisielewski M, Wierdak M, et al.[9] 2015 Poland	Randomized clinical trial	1B	To establish the influence of the preoperative intake of a carbohydrate-rich solution on the insulin resistance	The study analyzed 40 patients. Hyperglycemia and an increase in the cortisol levels were found in the immediate postoperative period,

			and cortisol levels in patients subjected to elective laparoscopic cholecystectomy.	with a decrease within 24 hours. The most expressive changes were found in the patients with longer fasting time (> 8 hours).
Bang P, Thorell A, Carlsson-Skwirut C, Ljungqvist O, Brismar K, Nygren J.[10] 2016 Sweden	Case-control study	3B	To investigate the hypothesis that shortened fasting promotes proteolysis of serum IGFBP-3-PA (Insulin-like growth factor binding protein *-3*), increases the bioavailability of circulating IGF-I (insulin-like growth factor), and preserves insulin sensibility when compared to the effects of extended fasting on elective colorectal surgery.	18 patients were analyzed. The oral carbohydrate solution ingested by the patients in the 2 hours prior to the surgery promoted an 18% improvement in insulin sensibility, greater IGFBP-3 proteolysis, and greater bioavailability of the circulating IGF-I in the postoperative period. The patients subjected to extended preoperative fasting presented greater postoperative insulin resistance.
Dilmen OK, Yenturb E, Tunalia Y, Balcic H, Bahar M.[11] 2017 Turkey	Case-control study	1B	To evaluate the metabolic effects of shortened fasting by the intake of a preoperative carbohydrate solution in lumbar disc surgery.	The study evaluated 43 ASA I-II patients. Groups of patients in extended and shortened preoperative fasting were compared. The was an increase in the cortisol and IL-6 levels in the postoperative period both in patients in extended fasting and in those in shortened fasting, with no significant difference. The study found that, regardless of the fasting time, insulin resistance was present in the postoperative period of lumbar disc surgeries.
Kreutzenberg S, Vigili D, Avogaro A.[12] 2017 Italy	Prospective cohort study	2B	To identify the serum levels of 3BOHB in patients with and without type 2 diabetes (DM2), before and after an elective coronary angiography; to detect the changes	A total of 38 patients (16 with diabetes and 22 without diabetes) were recruited for the study. A positive correlation was detected between fasting time and fasting plasma glucose levels (the longer the fasting

			in the 3BOHB levels during the procedure and to perform possible associations between 3BOHB and the clinical parameters/results obtained.	time, the greater the postoperative hyperglycemia condition). On the other hand, there was no association between fasting time and 3BOHB levels.
Burstal RJ, Reilly JR, Burstal B.[13] 2018 Australia	Prospective cohort study	2B	To investigate ketonemia and the relation between beta-hydroxybutyrate, glycemia, and preoperative fasting in non-diabetic adults subjected to extended fasting for elective or emergency surgeries.	In total, 100 patients were evaluated. No relation was observed between fasting time and the ketone or glucose levels. Hyperketonemia was identified in three of the 100 patients, one of whom ingested a ketogenic supplement the night before the surgery. No patient in extended fasting showed beta-hydroxybutyrate levels suggestive of ketoacidosis.
Hosny H, Desa MI, El-Siory W, Abdel-Monem A. [14] 2018 London	Case-control study	2B	To compare the metabolic effects of shortened fasting by means of a preoperative infusion of a lipid or carbohydrate emulsion to the conventional preoperative fasting (> 8 hours) on the postoperative insulin and free fatty acid (FFA) levels in obese patients subjected to myocardial revascularization.	The study was carried out with 63 patients. The most expressive metabolic changes were found in patients in extended fasting. The FFA, insulin, glucose, triglycerides, and VLDL levels were significantly lower in the group subjected to the shorter fasting time and that received the preoperative lipid infusion.
Reis PGA, Polakowski C, Lopes M, Bussyguin DS, Ferreira RP, Preti VB. [15] 2019 Brazil	Case-control study	2B	To evaluate the influence of shortened preoperative fasting on the outcomes of patients subjected to colorectal cancer surgery.	33 patients were included (15 in shortened fasting and 18 in conventional fasting). Shorter time to fully reach full feeding was required in patients in shortened fasting when compared to those in extended fasting (10 versus 16 days), noting that the

				shorter the fasting time, the better the nutritional metabolic recovery in postoperative patients.
Yeniay O, Tekgul ZT, Okur O, Koroglu N. [16] 2019 Turkey	Prospective observational study	2B	To measure the preoperative fasting time comparing it to the period of the day in which the procedure was carried out (morning, afternoon, and night), and to evaluate the effect of fasting on the vital parameters and electrocardiogram in aged patients subjected to elective surgery under spinal anesthesia.	211 patients were investigated. The mean fasting times were 12 ± 2.8 and 95 ± 2.1 hours in the morning group, and 15.5 ± 3.4 and 12.7 ± 4.4 in the afternoon group for food and liquid, respectively. ECG changes were significantly more frequent in the group with longer preoperative fasting time.
Wuensch T, Quint J, Mueller V, Mueller A, Wizenty J, Kaffarnik M, et al.[17] 2019 Germany	Prospective observational study.	2B	To investigate plasma markers sensible to the preoperative fasting time that allow for the metabolic characterization of surgical patients for a preoperative metabolic preparation optimized in patients subjected to gastrointestinal tract elective surgery.	50 patients were investigated. The patients with preoperative fasting time over 16 hours presented an increase in the plasma levels of valine, leucine, serine, a-amino butyric acid, free fatty acids, and 3-hydroxy butyric acid. Only valine and glutamic acid appear as independent metabolic markers for a precise prediction of changes related to extended fasting (in this case, more than or equal to 20 hours)
Liu B, Wang Y, Liu S, Zhao T, Zhao B, Jiang X, et al.[18] 2019 China	Randomized clinical trial	1B	To compare the metabolic effects induced by the shortened preoperative fasting, with ingestion of an oral carbohydrate solution two hours	The study evaluated 120 patients. The patients with longer preoperative fasting time presented an increase in the glycemic levels and greater insulin resistance when compared to those with

			before the surgical procedure and the extended preoperative fasting lasting more than eight hours in elective craniotomy.	shorter fasting time. Better glucose homeostasis was achieved in patients who ingested the oral carbohydrate solution during the preoperative period.

Source: Authors, 2020. IGFBP-3: Type 3 IGF-I binding protein; IGF-I: type 1 insulin-like growth factor; FFA: free fatty acid; VLDL: very low-density lipoprotein; 3BOHB: 3-hydroxybutyrate.

Eight studies (80%) found metabolic changes when evaluating the influence of shortened fasting, comparing groups in conventional preoperative fasting (8 to 12 hours) to groups subjected to shortened fasting time upon ingestion of a carbohydrate solution within two hours before the surgical procedure, according to what is proposed by programs for the optimization of postoperative recovery(9-15,18), while the other studies investigated the metabolic changes only in patients with extended fasting time, with no comparative analysis(16,17).

The results of the studies show the relation between the preoperative fasting time and the metabolic changes observed in the postoperative period, when the metabolic markers involved in the organic processes of response to surgical trauma oscillate, enhanced by the catabolic reactions promoted by the extended fasting time. The main clinical markers investigated and the respective metabolic changes found in the studies are described in Figure 3.

Figure 3: Metabolic changes and the relation with preoperative fasting time. Rio de Janeiro, RJ, Brazil, 2020.

Metabolic Marker	**Fasting time**	**Main changes**
Glucose	≥ 8 hours	(1) Progressive increase in serum glucose level from intraoperative to the first three hours after elective craniotomy. (2) Progressive increase in the glucose level from the immediate postoperative period, decreasing 24 hours after laparoscopic cholecystectomy.
Plasma insulin	≥ 8 hours	(1) Increase in the insulin level during the intraoperative period, decreasing progressively from 2 hours post-procedure, returning to the baseline levels three hours after the craniotomy. (2) Progressive increase in the insulin level from the immediate postoperative period up to 24 hours after the laparoscopic cholecystectomy.
Cortisol	≥ 8 hours	(1) Increase in the cortisol plasma levels two hours after the skin incision in lumbar discectomy. (2) Increase in plasma cortisol immediately after the laparoscopic

		cholecystectomy, with an expressive decrease 24 hours after procedure conclusion.
IGF-I IGFBP-3-PA	≥ 8 hours	A significant decrease in IGF-I and in the IGFBP-3 proteolysis, with a consequent increase in postoperative insulin resistance in patients subjected to abdominal surgery.
Valine	≥ 16-20 hours	Increase in the postoperative valine plasma concentration in patients subjected to gastrointestinal tract surgery.
Glutamic Acid	≥ 16-20 hours	Reduction in glutamic acid plasma levels in patients subjected to gastrointestinal tract surgery.
Interleukin 6 (IL-6)	≥ 8 hours	Increase in the IL-6 levels in the lumbar discectomy immediate postoperative period.

Source: Authors, 2020.

DISCUSSION

From the analysis of the selected articles, the results found were stratified into two categories according to the study objective.

1. Metabolic changes in the postoperative period of elective surgeries:

In the analysis of the primary results of the studies, glucose and insulin oscillated similarly, with an increase in the serum levels at the immediate postoperative period and a progressive drop in the first 24 hours in patients subjected to extended preoperative fasting[9,18].

When comparing the effects of conventional fasting to shortened fasting in the preoperative period of laparoscopic cholecystectomy, one study observed glucose and insulin increases in both; however, with no influence of the preoperative fasting time on the metabolic condition of the patients during and after the procedure[9].

Similar results were found in another study with patients subjected to laparoscopic cholecystectomy. No significant differences were found between the groups, a postoperative glycemic increase being found in both, with values between 129.67 ± 18.6 mg/dL in the traditional fasting group (>8 hours) and 124.34 ± 20.62 mg/dL in the shortened fasting group[19].

In major procedures such as non-laparoscopic gynecological surgeries, the glycemic increase was more expressive. In Brazil, a study identified a 55.19% increase in the postoperative glycemic level of patients in extended fasting, whereas in the shortened fasting group the glycemic increase was 32.53%, showing that shortening the preoperative fasting time reduces the organic answer to the trauma[20].

In fact, the metabolic changes provoked by extended preoperative fasting are proportional to the magnitude of the surgery, being more expressive in major surgical procedures[21].

In addition to changes in the postoperative glycemic levels, alterations in the secretion of the cortisol hormone are identified. Among the analyzed studies, two verified a significant increase in the cortisol serum levels in the immediate postoperative period of major and medium-size surgeries[9,11].

In the clinical practice, high cortisol levels in surgical patients can influence the postoperative insulin resistance levels and glycemic changes[22]. The increase of the cortisol secretion arises from the neuro-endocrine response produced by the organism after the surgical trauma, which corroborates the results found. They excessively stimulate the catabolic state that contributes to perioperative hyperglycemia and severe complications, such as diabetic ketoacidosis, or a non-ketotic hyperglycemic hyperosmolar state[23].

Insulin resistance develops during the surgery and is present for a long time in the postoperative period[23]. It can last up to three weeks after the performance of elective surgeries, with greater intensity on the first and second day of the postoperative period[24].

Another biomarker with possible relevance in the metabolic state of surgical patients is interleukin-6 (IL-6), a pro-inflammatory cytokine that mediates the immune response and acts on several cell types. It presents a positive correlation with insulin resistance and is found at high levels in chronic diseases like DM2[23].

One of the selected articles evaluated the effect of the ingestion of preoperative oral carbohydrates on insulin resistance and on the response to surgical stress after lumbar discectomy, using interleukin-6 as marker, verifying that the IL-6 plasma levels increased considerably after 24 hours of skin incision in the group subjected to conventional fasting[11].

A European research study, upon evaluation of the IL-6 levels in 137 patients in the pre- and postoperative periods, verified a high level of IL-6 (≥ 432 pg/mL), as well as a 3 times higher risk of postoperative complications and an increase in hospitalization time. Outcomes such as pneumonia, sepsis, anastomotic dehiscence, wound infection, mortality, and re-surgery were found[25].

Changes in the IGF-1 (insulin-like growth factor) and IGFBP-3 (IGF-1 binding protein 3) serum levels were also detected among patients with preoperative fasting times longer than eight hours. In the postoperative period of abdominal surgeries, 18 patients had a significant reduction in the IGF-I levels and in IGFBP-3 proteolysis, with a consequent increase in insulin resistance[10].

In contrast, patients in shortened fasting had an increase in IGF-I and in IGFBP-3 proteolysis, that is, lower circulating levels of free IGFBP-3 in plasma, indicating that the increased availability of IGF-I and the effects of IGF-I on glucose uptake are involved in the hormone mechanisms for a lower insulin resistance after the surgical trauma[10].

Another study identified a reduction in the IGFB-3 circulating levels by analyzing 80 patients subjected to mastectomy with reduced fasting time and who received a carbohydrate solution two hours before the surgery[26]. Despite these findings, there is a scarcity of updated studies addressing the effects of extended preoperative fasting on the IGF-1 and IGBP-3 levels and the consequences of these changes in the postoperative outcome in different medical specialties.

Metabolic effects of extended fasting on the valine and glutamic acid levels were reported in one of the studies included in this review, in which 50 patients in preoperative fasting for more than 16 hours, subjected to gastrointestinal surgery, presented an expressive increase in the plasma concentration of valine and a reduction in the postoperative glutamic acid levels[17].

A possible mechanism that causes the decline in glutamic acid throughout extended fasting is the hepatic catabolism of glutamic acid, intensified in this condition by an increase in the activity of glutamate dehydrogenase, an important enzyme in the hepatic regulation of nitrogen and energy metabolism, catalyzing one of the most relevant anaplerotic reactions[27].

In contrast, the valine levels increased as fasting time advanced, which can be explained by an increase in the degradation of muscle protein to provide the hepatic gluconeogenesis with substrates throughout the fasting period, since valine oxidation is increased in times of inadequate supply of amino acids[17].

No recent reports were found in the literature on the influence of valine and glutamic acid on the postoperative period and its relation with fasting time. Considering the results obtained by the analyzed study[17]. The publication of new studies that investigate the influence of preoperative fasting time on the valine and the glutamic acid levels, as well as the metabolic impact on the postoperative recovery, becomes relevant.

2. Relation of the postoperative metabolic changes with preoperative fasting time:

Extended preoperative fasting enhances the metabolic response to the surgical trauma[4]. The American Society of Anesthesiologists (ASA) recommends the conducts established by the ERAS and ACERTO multimodal protocols, anticipating fasting by ingesting clear liquids up to two hours and light meals up to six hours for healthy patients before elective surgical procedures that need general/local anesthesia or sedation/analgesia[28].

The ten articles reviewed addressed fasting time in their studies, in which six used the case-control method to compare which results were more beneficial to the patient[9-14]. These are studies coming from different nations, which demonstrates that the shortening of preoperative fasting is still little practiced, even with the advent of studies that prove its effectiveness.

In the case-control studies that compared patients in traditional fasting (more than 8 hours) to patients in shortened fasting (six hours for solids and two hours for liquids), it was possible to note that the fasting time reflects the reality of many hospital institutions, where the relation between time and the fasting prescribed and practiced is disproportionate(29). In these articles, it was evidenced that fasting with a mean of two hours for clear fluids, including carbohydrate-rich beverages, reduced the postoperative metabolic changes(9-14).

In fact, the reduction in fasting time promotes a safer and more beneficial postoperative period to the patients. When observing the implementation of the ERAS protocols to hepatic surgery in a Brazilian tertiary care center, in the group of patients subjected to ERAS, a reduction in preoperative fasting time was observed (six hours for solids and two hours for liquids) and, consequently, a two-day reduction in the postoperative hospitalization time(30).

The fasting time recommended by the studies was at least eight hours for food and liquid. In Brazil, when evaluating the clinical, surgical, and nutritional profile of 140 surgical patients admitted in a reference hospital, the median of the preoperative fasting time obtained for minor surgeries was 15 hours, while for medium-complexity surgeries was 13.5 hours, which demonstrates non-conformity with the new guidelines. The study also found that malnourished patients presented longer pre- and postoperative fasting and hospitalization time when compared to those well-nourished(31).

In Argentina, the fasting time established by institutions also surpasses the recommendations of the current guidelines. In a study with 139 patients, the mean of the preoperative fasting time prescribed was 12.5 hours, both for solids and liquids, while the actual fasting had a mean of 14 hours for solid food, being longer than prescribed. In comparison to the recommendation of the AAARBA *(Asociación de Anestesia, Analgesia y Reanimación de Buenos Aires)* guidelines, prescribed fasting exceeded the 4.5-hour recommendation for solids and 10.5 for liquids, not fitting into the current recommendations(32).

One of the articles selected, published in Germany, reports the length of preoperative fasting for a mean time that varied between 16 and 20 hours(16). Another study from Turkey compared the time of the day in which the surgery was carried out to the effect of fasting time on an elective surgery. The fasting means were 12 ± 2.8 and 9.5 ± 2.1 hours in the morning group and

15.5 ± 3.4 and 12.7 ± 4.4 in the afternoon group for solids and liquids, respectively. The greatest changes occurred in the group with longer fasting time[16].

Therefore, preoperative fasting time has a direct relation proportional to the occurrence of postoperative metabolic changes. Shortening preoperative fasting minimizes postoperative metabolic changes, promoting greater comfort and less organic stress to the patient, as well as a reduction in hospitalization time and morbidity[15,16,24].

This study has as a limitation the time frame of publications within the last five years, which made it impossible to select some articles found. The expansion of Brazilian studies on this study object is recommended.

CONCLUSION

The main metabolic changes found were hyperglycemia, increase in the IL-6, cortisol, and valine levels, increase in insulin resistance, reduction in the glutamic acid plasma levels and increase in the IGF-1 levels with a reduction of IGFBP-3.

A direct relation was verified between preoperative fasting time and the occurrence of postoperative metabolic changes. The studies show that reducing preoperative fasting time minimizes postoperative metabolic changes, promoting less organic stress to the patient, and a reduction in hospitalization time and morbidity.

The results found in this study corroborate for a reformulation of the care practices for the surgical patient, by reducing preoperative fasting time, providing the patient with greater comfort and well-being, reducing sensations of thirst and hunger, in addition to a safer clinical/metabolic post-surgery outcome.

REFERENCES:

1. Barbosa MV, Queiroz FM, Pinho NB, Martucci RB. Impact of the use of immunomodulatory diet in colorectal cancer patients under elective surgeries with preoperative fasting abbreviation. Rev Bras Cancerol 2015 Jul/Sep [cited 04 Sep 2020];61(3):217-225. Available from: https://pesquisa.bvsalud.org/portal/resource/pt/biblio-833859.
2. Martins AJC, Serva CAS, Fonseca TH, Martins MJL, Poveda VB. Fasting of less than eight hours in urgent and emergency surgeries versus complication. Rev Bras de Enferm 2016 Nov;69(4):712-7. Doi: https://doi.org/10.1590/0034-7167.2016690414i.
3. Aguilar-Nascimento JE, Salomão AB, Waitzberg DL, Dock-Nascimento DB, CORREA MITD, Campos ACL, et al. Acerto guidelines of perioperative nutritional interventions period in elective general surgery. Rev Col Bras Cir 2017 Dec;44(6):633-648. Doi: https://doi.org/10.1590/0100-69912017006003.
4. Carvalho CALB, Carvalho AA, Nogueira PLB, Aguilar-Nascimento JE. Changing paradigms in preoperative fasting: results of a joint effort in pediatric surgery. Arq Bras Cir Dig 2017 Jan/Mar;30(1):7-10. Doi: https://doi.org/10.1590/0102-6720201700010003.
5. Mendes KDS, Silveira RCCP, Galvao CM. Integrative literature review: a research method to incorporate evidence in health care and nursing.

Text Context Enferm 2008 Oct/Dec;17(4):758-764. Doi: https://doi.org/10.1590/S0104-07072008000400018.
6. The Joanna Briggs Institute. Joanna Briggs Institute Reviewers' Manual: 2015 [cited 13 Jul 2020]. 2015. p. 7. Available from: https://nursing.lsuhsc.edu/JBI/docs/ReviewersManuals/Scoping-.pdf.
7. Oxford Centre for Evidence-based Medicine: levels of evidence [Internet]. 2009 Mar [cited 2014 dez 20]. Available from: http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009.
8. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. Epidemiol. Serv. Saúde 2015 Jun;24(2):335-342. Doi: https://doi.org/10.5123/S1679-49742015000200017.
9. Pędziwiatr M, Pisarska M, Matłok M, Major P, Kisielewski M, Wierdak M, et al. Randomized Clinical Trial to Compare the Effects of Preoperative Oral Carbohydrate Loading versus Placebo on Insulin Resistance and Cortisol Level after Laparoscopic Cholecystectomy. Polski Przegląd Chirurgiczny. 2015 Aug;87(8):402–408. Doi: https://doi.org/10.1515/pjs-2015-0079. [incluída na revisão]
10. Bang P, Thorell A, Carlsson-Skwirut C, Ljungqvist O, Brismar K, Nygren J. Free dissociable IGF-I: Association with changes in IGFBP-3 proteolysis and insulin sensitivity after surgery. Clinical Nutrition 2016 Mar;(35):408-413. Doi: https://doi.org/10.1016/j.clnu.2015.03.003. [incluída na revisão]
11. Dilmen OK, Yenturb E, Tunalia Y, Balcic H, Bahar M. Does preoperative oral carbohydrate treatment reduce thepostoperative surgical stress response in lumbar disc surgery? Clinical Neurology and Neurosurgery 2017 Dec;(153):82–86. Doi: https://doi.org/10.1016/j.clineuro.2016.12.016. [incluída na revisão]
12. Kreutzenberg S, Vigili D, Avogaro A. The role of point-of-care 3-hydroxybutyrate testing in patients with type 2 diabetes undergoing coronary angiography. J Endocrinol Invest 2017 Feb;(40):627–634. Doi: https://doi.org/10.1007/s40618-017-0615-0. [incluída na revisão]
13. Burstal RJ, Reilly JR, Burstal B. Fasting Or Starving? Measurement of Blood Ketone Levels in 100 Fasted Elective and Emergency Adult Surgical Patients at An Australian Tertiary Hospital. Anaesth Intens Care 2018 Sep;46(5):463-467. Doi: https://doi.org/10.1177/0310057X1804600506. [incluída na revisão]
14. Hosny H, Desa MI, El-Siory W, Abdel-Monem A. Comparative Study Between Conventional Fasting Versus Overnight Infusion of Lipid or Carbohydrate on Insulin and Free Fatty Acids in Obese Patients Undergoing Elective On-pump Coronary Artery Bypass Grafting. A Prospective Randomized Trial. Journal of Cardiothoracic and Vascular Anesthesia 2018 Jun;(32):1248–1253. Doi: https://doi.org/10.1053/j.jvca.2017.11.020. [incluída na revisão]
15. Reis PGA, Polakowski C, Lopes M, Bussyguin DS, Ferreira RP, Preti VB. Abbreviated preoperative fasting favours postoperative oral intake at lower hospital admission costs for cancer patients. Rev Col Bras Cir 2019 Aug;46(3):e20192175. Doi: https://doi.org/10.1590/0100-6991e-20192175. [incluída na revisão]
16. Yeniay O, Tekgul ZT, Okur O, Koroglu N. Unexpectedly prolonged fasting and its consequences on elderly patients undergoing spinal anesthetics. A prospective observational study. Acta Cir Bras 2019 Mar;34(3):e201900309. Doi: https://doi.org/10.1590/s0102-865020190030000009. [incluída na revisão]
17. Wuensch T, Quint J, Mueller V, Mueller A, Wizenty J, Kaffarnik M, et al. Identification of serological markers for pre and postoperative fasting periods. Clin Nutr ESPEN 2019 Apr;(30):131-137. Doi: https://doi.org/10.1016/j.clnesp.2019.01.004. [incluída na revisão]
18. Liu B, Wang Y, Liu S, Zhao T, Zhao B, Jiang X, et al. A randomized controlled study of preoperative oral

carbohydrate loading versus fasting in patients undergoing elective craniotomy. Clin Nutr 2019 Nov;38(5):2106-2112. Doi: https://doi.org/10.1016/j.clnu.2018.11.008. [incluída na revisão]
19. Udayasankar M, Udupi S, Shenoy A. Comparison of perioperative patient comfort with 'enhanced recovery after surgery (ERAS) approach' versus 'traditional approach' for elective laparoscopic cholecystectomy. Indian J Anaesth 2020 Apr;64(4):66-71. Doi: https://doi.org/10.4103/ija.IJA_782_19.
20. Marquini GV, Pinheiro FES, Vieira AUC, Pinto RMC, Uyeda MGBK, Batista MJ, et al. Preoperative fasting abbreviation (Enhanced Recovery After Surgery protocol) and its effects on the metabolism of patients undergoing gynecologic surgeries under spinal anesthesia: A randomized clinical trial. Nutrition 2020 Mar;77:110790. Doi: https://doi.org/10.1016/j.nut.2020.110790.
21. Jovanovski-Srceva M, Kuzmanovska B, Mojsova M, Kartalov A, Shosholcheva M, Temelkovska-Stevanoska M, et al. Insulin resistance, glycemia and cortisol levels in surgical patients who had preoperative caloric load with amino acids. Prilozi (Makedonska Akademija na Naukite i umetnostite. Oddelenie za Medicinski Nauki) 2015 Jan;36(3):61-70. Doi: https://doi.org/10.1515/prilozi-2015-0079.
22. Dogra P, Jialal I. Diabetic Perioperative Management. Dasgupta A, Sepulveda JL. Accurate Results in the Clinical Laboratory: a guide to error detected and correction. Elsevier 2 ed. 2020. p. 165-189. Available from: https://www.ncbi.nlm.nih.gov/books/NBK540965/.
23. Pontes JPJ, Mendes FF, Vasconcelos MM, Batista NR. Evaluation and perioperative management of patients with diabetes mellitus. A challenge for the anesthesiologist. Rev Bras Anestesiol 2018 Jan/Feb;68(1):75-86. Doi: https://doi.org/10.1016/j.bjan.2017.04.017.
24. Marcarini M, Rosa SC, Wieck FP, Betti AH. Reduced preoperative fasting time: the perioperative clinical aspects related to cardiac surgical patients. Braspen J 2017 Oct/Dec [cited 08 Jun 2020];32(4):375-379. Available from: https://pesquisa.bvsalud.org/portal/resource/pt/biblio-906846.
25. Rettig TCD, Verwijmeren L, Dijkstra IM, Boerma D, Van de Garde EMW, Noordzij PG. Postoperative Interleukin-6 Level and Early Detection of Complications After Elective Major Abdominal Surgery. Ann Surg 2016 Jun;263(6):1207-12. Doi: https://doi.org/10.1097/SLA.0000000000001342.
26. Gutefeldt K, Hedman CA, Thyberg ISM, Bachrach-Lindström M, Spångeus A, Arnqvist HJ. Dysregulated Growth Hormone-Insulin-Like Growth Factor -1 Axis in Adult Type 1 Diabetes with Long Duration. Clinical Endocrinology 2018 Jul;89(4):424-430. Doi: https://doi.org/10.1111/cen.13810.
27. Lende TH, Austdal M, Varhaugvik AE, Skaland I, Gudlaugsson E, Kvaløy JT. Influence of pre-operative oral carbohydrate loading vs. standard fasting on tumor proliferation and clinical outcome in breast cancer patients — a randomized trial. BMC Cancer 2019 Nov;(19):1076. Doi: https://doi.org/10.1186/s12885-019-6275-z.
28. Vázquez-Martínez O, Méndez I, Turrubiate I, Valente-Godínez H, Pérez-Mendoza M, García-Tejada P, Díaz-Munõz M. Restricted feeding modulates the daily variations of liver glutamate dehydrogenase activity, expression, and histological location. Exp Biol Med (Maywood) 2017 May;(242):945e52. Doi: https://doi.org/10.1177/1535370217699533.
29. Azevedo SCL, Campos SBG; Meira JEC; Guedes GS. Abreviação do jejum pré-operatório: protocolo multimodal baseado em evidência. Gep News, 2017 Jul/Set [cited 2020 Jul 14];1(3):11-13. Available from: https://www.seer.ufal.br/index.php/gepnews/article/view/3495.
30. Francisco SC, Batista ST, Pena GG. Fasting in elective surgical patients: comparison among the time prescribed, performed and recommended on perioperative care protocols. ABCD Arq Bras Cir Dig 2015

Nov/Dec;28(4):250-254. Doi: https://doi.org/10.1590/S0102-6720201500040008.

31. Teixeira UF, Goldoni MB, Waechter FL, Sampaio JA, Mendes FF, Fontes PR. Enhanced recovery (ERAS) after liver surgery: comparative study in a Brazilian terciary center. ABCD Arq Bras Cir Dig 2019 Feb;32(1):e1424. Doi: https://doi.org/10.1590/0102-672020180001e1424.
32. Lucchesi FA, Gadelha PCFP. Nutritional status and evaluation of the perioperative fasting time among patients submitted to elective and emergency surgeries at a reference hospital. Rev Col Bras Cir 2019 Oct;46(4):e20192222. Doi: https://doi.org/10.1590/0100-6991e-20192222.
33. Milagros De Luca, Cecilia Mabel Maidana, Denise Moscardi Pietrasanta, Sandra Viviana Velazquez y Patricia Laura Ruscitti. Duración del ayuno preoperatorio en pacientes con cirugía programada. Rev. Hosp. Ital. B. Aires 2019 Sept [cited 17 Oct 2020];39(3):77-80. Available from: https://pesquisa.bvsalud.org/portal/resource/pt/biblio-1048219.