Volume 9, No. 4, July 2019 * Bimonthly

ISSN: 2251-9939

Journal of Life Science and Biomedicine

Available online at www.jlsb.science-line.com

Published by
Scienceline Publications

Journal of Life Science and Biomedicine

(2251-9939)

J. Life Sci. Biomed. 9 (4): 82-121, July 25, 2019

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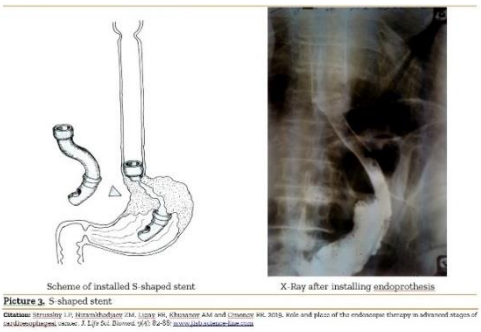
Volume 9 (4); July 25, 2019

Research Paper

Role and place of the endoscopic therapy in advanced stages of cardioesophageal cancer.

Strusskiy LP, Nizamkhodjaev ZM, Ligay RE, Khusanov AM and Omonov RR.
J. Life Sci. Biomed., 9(4): 82-88, 2019;
pii:S225199391900013-9



Abstract
Aim. The aim of study was to investigate efficacy of palliative treatment of proximal gastric tumors. **Methods.** The article describes experience of treating 232 patients with unresectable cardioesophageal cancer (UCC). Of these, minimally invasive endoscopic procedures: endoscopic diatermotunnelization (ED), endoscopic bougienage (EB) and endoscopic stenting (ES) was performed in 101 patients. Currently, the method of endoscopic stenting is preferred, which was performed in 84 patients, and own-developed model of a silicone tube stent was used in all patients. Main early and late complications of using this method were described. **Results.** Minimally invasive techniques described, the absence of a cosmetic defect, there is no need of specific care set endoprothesis and relatively easily tolerated by patients of the technique endoprosthetic stent installation suggest a viable alternative to the imposition of gastrostomy and jejunostomy.

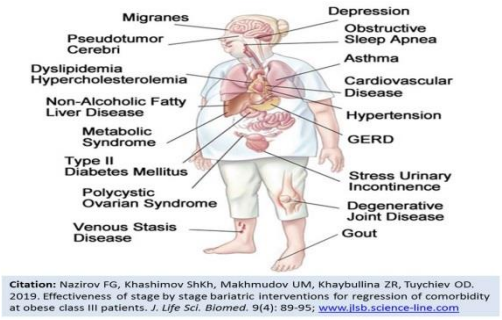
Keywords: Tumours of the proximal part of the stomach, Surgical treatment, Unresectability, Invasive technologies, Diathermotunnelization, Endoscopic bougienage, Endoscopic stenting.

[Full text-PDF] [XML]

Research Paper

Effectiveness of stage by stage bariatric interventions for regression of comorbidity at obese class III patients.

Nazirov FG, Khashimov ShKh, Makhmudov UM, Khaybullina ZR, Tuychiev OD.
J. Life Sci. Biomed., 9(4): 89-95, 2019;
pii:S225199391900014-9



Abstract
Introduction. Currently obesity is considered as a chronic, relapsing, multifactorial neurobehavioral disease, in which an increase in body fat contributes to the dysfunction of adipose tissue and the biomechanical effect of adipose tissue on surrounding tissue with development of metabolic and psychosocial health effects. It has been proven that bariatric surgery significantly reduces the level of pro-inflammatory senility-associated secretory proteins (SASPs), weight reduction increases telomeres length and declines their oxidative degradation (lowering of oxidative stress in telomeres), miR10a_5p, which is post-regulated with increasing of biological age, decreased after surgery, what suggests that bariatric surgery abated the premature aging phenotype. It is of big interest to evaluate comorbidity conditions in people with obese class III after the intervention of intragastric balloons (IGB) and laparoscopic sleeve gastrectomy (LSG), which are lead to weight loss. **Methods.** A total of 40 patients (32 female and 8 male aged 19–55 years were considered for the study. Comorbidity was assessed by the structure and severity of diseases associated with obesity according to the recommendations of Nedogoda (2016). Cardiometabolic disease staging scale of Guo (2015) was used to assess the metabolic health. Endovisual surgery-LSG was performed (n=40) on a laparoscopic set and instruments of Karl Storz, GMBH & CoKG (Germany). The spherical intragastric balloon (IGB) was installed according to the manufacturer's method (BIB ™ System Intragastric Balloon from Allergan Inc. USA) using a GIF-1T20 Olympus gastrointestinal fibroscope (Japan). **Results.** Evaluation of the obesity phenotype, a completely metabolically healthy phenotype was not detected in any case. Nowadays, the opinion about the usefulness of the clinical concept of the metabolic syndrome (MS) is disputed, because it has not been convincingly proven its predictive value exceeds that for individual components. **Conclusion.** Obese class III is associated with dyslipidemia/hypertriglyceridemia in 85%; with type 2 diabetes mellitus (DM2)/prediabetes in 50%; with arterial hypertension (AH) in 45%; and with non-alcoholic fatty liver disease (NAFLD) in 35% of cases. Therefore, two-stage treatment by IGB and LSG make it possible to improve the performance on the Cardiometabolic disease staging scale, achieving zero cardiometabolic risk in 35% of patients, and in rest of patients move to a lower stage.

Keywords: Obesity, Bariatric surgery, Comorbidity, Intragastric balloon, Endovisual surgery.

[Full text-PDF] [XML]

Research Paper

Characteristics and early clinical outcomes of patients undergoing living-related kidney transplantation.

Nazirov FG, Bakhritdinov FSh, Ibadov RA, Matkarimov ZT, Suyumov AS, Sobirov JG, Ibragimov SKh.
J. Life Sci. Biomed., 9(4): 96-101, 2019;
pii:S225199391900015-9

Abstract
Aim. This study aimed to access early outcomes of living-related kidney transplantation. **Methods.** The results of treatment of 159 patients (135 males and 24 females) with chronic renal disease during 2010- 2018, have been investigated. Two new and traditional methods have been studied. New optimized method was performed for the main group (n=98) observed since February 2018, while the comparison group (n=61) from 2010 to February 2018 was operated in the traditional way. The characteristics of the patients were compared using the Wilcoxon rank-sum test or the Fisher's exact test as appropriate. All tests were two-sided, and P<0.05 was considered statistically significant. Analyses were performed using the R statistical package. **Results.** In 149 (93.7%) cases, the functional activity of the kidney transplants was assessed as a primary functioning graft with 95 (96.9%) cases in the main group and 54 (88.5%) in comparison group (P=0.048). Delayed graft function was detected in 2 (2.0%) recipients of the main group and in 5 (8.2%) cases of the comparison group. In the postoperative period, a significant decrease in creatinine level was observed in the main group of recipients and on the 1st day it was 221.0±58.7μmol/L, whereas in the comparison group the index was 569.3±84.6 μmol/L (P<0.001). 3-4 days after surgery, the level of blood creatinine in the main group was significantly (P<0.01) lower than the comparison group (149.6±25.6 vs. 343.6±69.4 μmol/L). On the first day after surgery, there was also a significant decrease (P<0.05) in urea level of the main group (11.4±1.61 mmol/L) in comparison with the comparative group (15.4±0.84 mmol/L). At the time of hospital discharge of recipients, the level of urea was within normal limits and equal to 8.3±0.80 mmol/L and 9.0±0.95 mmol/L in the main and comparison groups, respectively (P>0.05). Hemodialysis was required in 3 (3.1%) recipients from the main group and 3 (4.9%) from the comparison group. The need for corticosteroid therapy was observed in 2 (2.0%) cases of the main group and in 3 (4.9%) cases from the comparison group. **Conclusion.** The effectiveness of improved approaches to patient management and surgical tactics of related kidney transplantation has been proved, taking into account the verification of the graft functional activity on the main clinical and biochemical data of the terminal stage of chronic renal failure regression.

Keywords: Kidney Transplantation, Living-Related Renal Transplant Recipients, Early Clinical Outcomes

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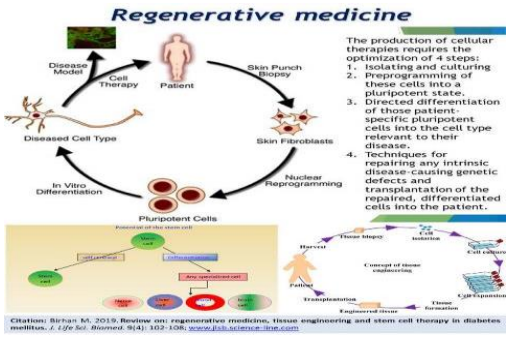
Review

Review on: regenerative medicine, tissue engineering and stem cell therapy in diabetes mellitus.



Birhan M.
J. Life Sci. Biomed., 9(4): 102-108, 2019;
pii:S225199391900016-9

Abstract
Introduction. In view of the recent success in pancreatic islet transplantation, interest in treating diabetes by the delivery of insulin-producing β-cells has been renewed. Because differentiated pancreatic β-cells cannot be expanded significantly *in vitro*, β-cell stem or progenitor cells are seen as a potential source for the preparation of transplantable insulin-producing tissue. In addition to embryonic stem (ES) cells, several potential adult islet/β-cell progenitors, derived from pancreas, liver, and bone marrow, are being studied. To date, none of the candidate cells has been fully characterized or is clinically applicable, but pancreatic physiology makes the existence of one or more types of adult islet stem cells very likely. It also seems possible that pluripotential stem cells, derived from the bone marrow, contribute to adult islet neogenesis. **Aim.** In future studies, more stringent criteria should be met to clonally define adult islet/β-cell progenitor cells. If this can be achieved, the utilization of these cells for the generation of insulin-producing β-cells in vitro seems to be feasible in the near future. This review will focus on the potential of adult tissue-derived stem cells, in lieu of embryo-derived stem cells, for the treatment of diabetes. We discuss the role of adult islet stem/progenitor cells in normal physiology, highlight possible candidate cells isolated to date, and describe different approaches for stem cell-based therapy.

Keywords: Embryonic Stem Cells, Insulin-Producing, Pancreatic Islet, Physiology, β-cells

[Full text-PDF] [XML]

Research Paper

Comparison of two methods of anterior cruciate ligament reconstruction with lavsan (polyethylene terephtalate).

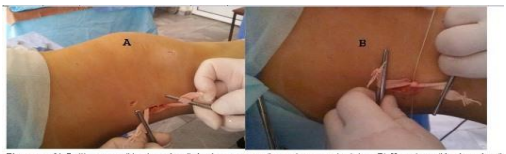


Figure 2. A) Pulling out of both ends of the lavsan tape from the same incision; B) Knotting of both ends of lavsan tapes.

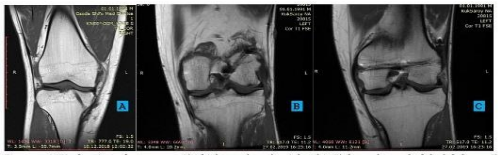


Figure 3. MRI of patient after surgery. A) tibial tunnel on the right tibia;B) femoral tunnel of the left femur;C) transversal tunnel of femur of left femur.

Citation: Irismetov ME, Usmonov FM, Shamshimetov DF, Kholikov AM, Rajabov KN, Tadjinazarov MB. 2019. Comparison of two methods of anterior cruciate ligament reconstruction with lavsan (polyethylene terephtalate). *J Life Sci Biomed*, 2019; 9(4): 109-116; www.jlsb.science-line.com

Irismetov ME, Usmonov FM, Shamshimetov DF, Kholikov AM, Rajabov KN, Tadjinazarov MB.
J. Life Sci. Biomed., 9(4): 109-116, 2019;
pii:S225199391900017-9

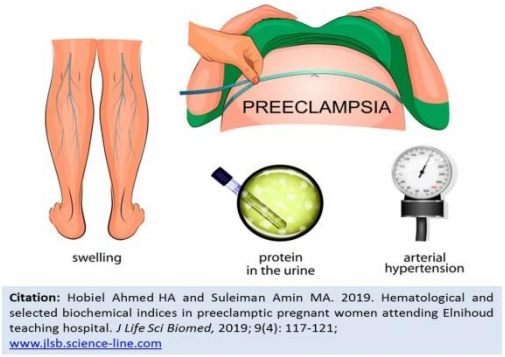
Abstract
Introduction. The anterior cruciate ligament (ACL) is one of the main stabilizateur of the knee joint. Many methods were suggested for its reconstruction with different allo/autografts, as well as synthetic materials. **Aim.** The study aimed to compare two methods of ACL reconstruction with lavsan (polyethylene terephtalate). **Methods.** The study included 102 patients who underwent ACL reconstruction with lavsan tape (polyethylene terephtalate). Group 1 (46 patients) underwent single-bundle ACL reconstruction, and group 2 (56 patients) underwent double-bundle reconstruction. Patients were evaluated with Lachman, anterior drawer and pivot-shift tests and Lysholm score. **Results.** Our results showed better results in double-bundle group, especially rotational stability was significant better. Besides that majority of patients of I group had some problem flexion of the operated knees. **Conclusion.** Independent of the method of ACL reconstructions these surgeries must be perform taking into account anatomic features and changes of the knee. Double-bundle technique of ACL reconstruction with lavsan provides better stability than single-bundle technique.

Keywords: Anterior Cruciate Ligament, Single-Bundle Technique, Double-Bundle-Technique, Synthetic Material

[Full text-PDF] [XML]

Research Paper

Hematological and selected biochemical indices in preeclamptic pregnant women attending Elnihoud teaching hospital.



Citation: Hobiel Ahmed HA and Suleiman Amin MA. 2019. Hematological and selected biochemical indices in preeclamptic pregnant women attending Elnihoud teaching hospital. *J Life Sci Biomed*, 2019; 9(4): 117-121; www.jlsb.science-line.com

Hobiel Ahmed HA and Suleiman Amin MA.
J. Life Sci. Biomed., 9(4): 117-121, 2019;
pii:S225199391900018-9

Abstract
Background. Preeclampsia (PE) is a form of hypertensive disorder of pregnancy, leading to maternal and perinatal morbidity and mortality worldwide. It is major obstetric problem in developing countries and affecting 2–10% of all pregnancies. **Aim.** This study aimed to evaluate hematological and some biochemical parameters in preeclamptic pregnant women attending Elnihoud Teaching Hospital, Sudan, and to compare the findings with the severity of the disease. **Methods.** A descriptive cross sectional study was carried out in Elnihoud Teaching Hospital with total of forty tow pregnant women as participants (14–45 years old). They were selected from the Wards of the Hospital at admission before starting treatment. Hematological and selected biochemical parameters were measured and analyzed for every preeclamptic patient. **Results.** The study revealed no significant elevation in plasma total protein, total white blood cells (TWBCs), lymphocytes and mean corpuscular volume (MCV) among severe preeclamptic patients versus mild cases. Decrease with no significant value in hemoglobin level, platelets count (PLT), red blood cells (RBCs) and mean corpuscular hemoglobin (MCH) was observed in severe preeclamptic cases compared to mild preeclamptic cases. **Conclusion.** It is concluded that measurement of hematological and some biochemical parameters might reflect to some extent the effect of preeclampsia on pregnant women. **Recommendation.** Further studies with more parameters can provide guidance for the evaluation intervention and management of pregnant women who suffering from PE.

Keywords: Preeclampsia, Hypertension, Proteinuria, Papillodema.

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Journal of Life Science and Biomedicine

ISSN: 2251-9939

Frequency: Bimonthly

Current Issue: 2019, Vol: 9, Issue 4 (July)

Publisher: SCIENCELINE

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2019 SCIENCELINE
Journal of Life Science and Biomedicine
J Life Sci Biomed, 9 (4): 82-88, 2019

ISSN 2251-9939

Role and place of the endoscopic therapy in advanced stages of cardioesophageal cancer

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ABSTRACT

Aim. The aim of study was to investigate efficacy of palliative treatment of proximal gastric tumors. Methods. The article describes experience of treating 232 patients with unresectable cardioesophageal cancer (UCC). Of these, minimally invasive endoscopic procedures: endoscopic diatermotunnelization (ED), endoscopic bougienage (EB) and endoscopic stenting (ES) was performed in 101 patients. Currently, the method of endoscopic stenting is preferred, which was performed in 84 patients, and own-developed model of a silicone tube stent was used in all patients. Main early and late complications of using this method were described. Results. Minimally invasive techniques described, the absence of a cosmetic defect, there is no need of specific care set endoprothesis and relatively easily tolerated by patients of the technique endoprosthetic stent installation suggest a viable alternative to the imposition of gastrostomy and jejunostomy.

Original Article
PII: S225199391900013-9

Rec.	13 March 2019
Rev.	18 June 2019
Pub.	25 July 2019

Keywords
**Tumours of the proximal part of the stomach,
Surgical treatment,
Unresectability,
Invasive technologies,
Diathermotunnelization,
Endoscopic bougienage,
Endoscopic stenting.**

INTRODUCTION

In spite of the steady decline in the incidence and mortality of gastric cancer remains extremely relevant problem [1-4]. For a long time this terrible disease was the leading cause of death from cancer pathology worldwide. Over the past 20 years, against a background of reducing the overall incidence of cancer of the stomach, marked by a sharp increase in the incidence of cancer cardio-esophageal region [4-8].

Among all sites of tumor lesions of the stomach cardioesophageal zones occupy from 10 to 37% [9, 10]. The main reason for the treatment of patients for medical treatment when cancer is cardioesophageal dysphagia, which progression occurs much faster than in benign narrowing [11-14]. Carried out before: gastrostomias & Yeyunostomia and ensure minimal invasiveness and adequacy of enteral nutrition.

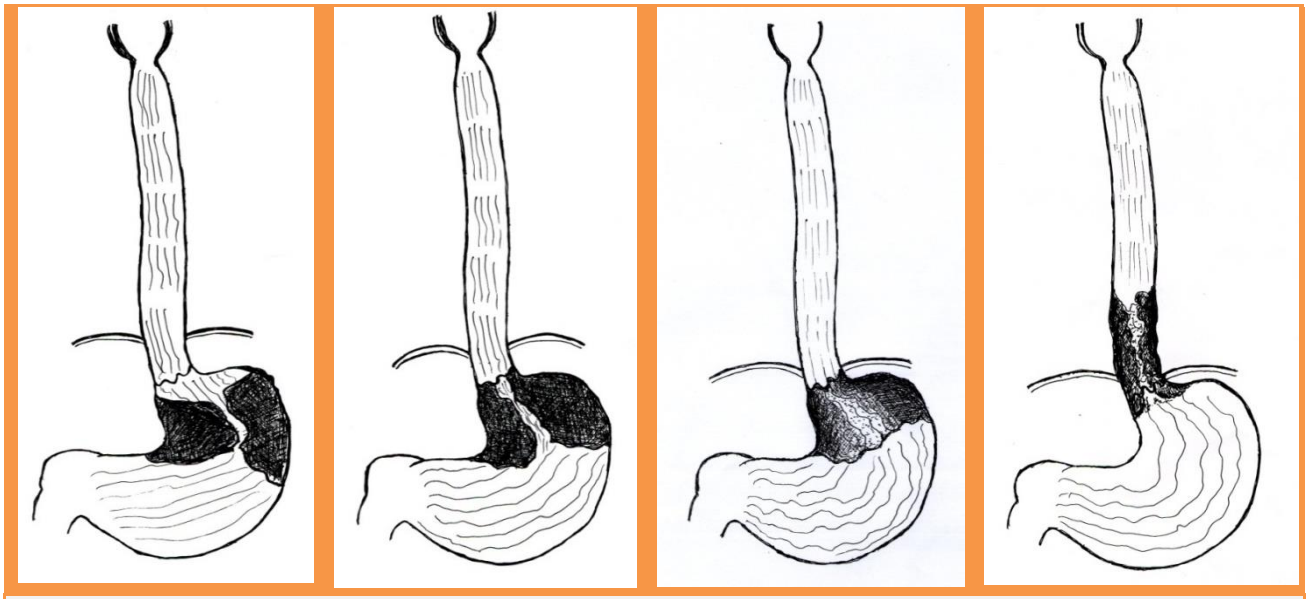
The introduction into clinical practice of minimally invasive technologies have greatly reconsider the tactics of treatment of patients with unresectable stage cardioesophageal tumors, which are aimed at improving the quality of the remaining life of patients and meet two basic requirements: minimum trauma and preserving the natural oral feeding. Objective of study was to examine the results of minimally invasive endoscopic treatment of patients with inoperable and unresectable stage cardioesophageal tumors.

MATERIAL AND METHODS

In the period from 2001 to 2014, in the department of surgery of the esophagus and the stomach of "RSCS them. Acad. V.Vahidova" were hospitalized 444 patients with tumors of the proximal stomach. Men was 333 (75%), and women was 111 (25%). Patients underwent a comprehensive study, which included endoscopy, radiopaque polypositional study of the esophagus and stomach, ultrasound of the abdomen, Multi-slice computed tomography (MSCT) and morphological study of biopsy specimens and macropreparations. In accordance with the classification of tumors cardioesophageal patients were distributed as follows:

Type I - adenocarcinoma of the distal esophagus with the ability to spread in the direction of the stomach - 115 (25.9%) patients; **Type II** - a true adenocarcinoma of the gastroesophageal transition zone (true cancer of the cardia) - 75 (16.9%) patients; **Type III** - a cancer of the localization of the main array subcardial tumors of the stomach and the possible involvement of the distal esophagus - 254 (57.2%) patients. Distribution of patients according to the extent of the cardioesophageal junction (CEJ) and the distal esophagus is presented in figure 1.

One of the first reasons for the treatment of patients with dysphagia was, in connection with which it analyzed the degree of tumor spread to the esophagus and the cortical evoked responses (CEP), which is presented in table 1. Only 93 (20.9%), dysphagia clinic was not, and in the majority of cases - 351 (79.1%) had dysphagia varying degrees of severity.



A: With the spread of the esophagus and the CET N=82 (18.5%)	**B:** Spread on the CEJ N=124 (27.9%)	**C:** With the transition to the abdominal esophagus N=167 (37.6%)	**D:** With the transition to the lower third of the thoracic N=71 (15.9%)

Figure 1. Distribution of patients according to the extent of the cortical evoked responses (CEP) and the distal esophagus. CEJ=cardioesophageal junction, CET= complete esophageal transit

Table 1. Degree of tumor spread

The degree of dysphagia	Prevalence in the CET and the esophagus				Total
	CET	abdominal esophagus	l/3 thoracic esophagus	Absolute	
No dysphagia	11(8.9%)	18(10.8%)	2(2.8%)	62(75.6%)	93(20.9%)
I degree	42(33.9%)	46(27.5%)	17(23.9%)	11(13.7%)	116(26.1%)
II degree	64(51.6%)	89(53.3%)	33(46.5%)	9(10.9%)	195(43.9%)
III degree	6(4.8%)	12(7.2%)	13(18.3%)	-	31(6.9%)
IV degree	1(0.8%)	2(1.2%)	6(8.5)	-	9(2%)
Total	124	167	71	82	444(100%)

CET= complete esophageal transit

Ethical approval

The review board and ethics committee of RSCS named after acad. V.Vakhidov approved the study protocol and informed consents were taken from all the participants.

RESULTS AND DISCUSSION

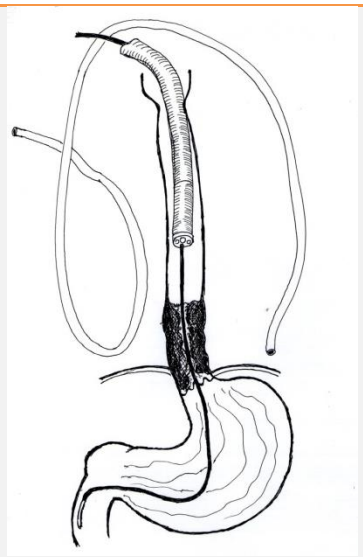
Of 444 patients, resection procedures were performed in 212 (47.7%) patients. The remaining 232 (52.3%) due to various reasons the process is recognized as inoperable or unresectable. This category of patients is devoted to the study. In 122 of 232 patients, which accounted for 52.6% of inoperable established on the basis of a comprehensive survey, while 110 (47.4%) only after laparotomy or laparoscopy. Summary of therapeutic measures is shown in table 2.

Symptomatic treatment was performed in 128 patients, which accounted for 55.2%. All patients were discharged to conduct a specific treatment in oncological institutions. Gastrostomy used only in 3 (1.3%) cases. Minimally invasive procedures were performed in 101 (43.5%) patients. Patients with dysphagia 3-4 degree and pronounced alimentary cachexia, as a preliminary preparation for the restriction zone was conducted nasogastric feeding controlled by endoscopy.

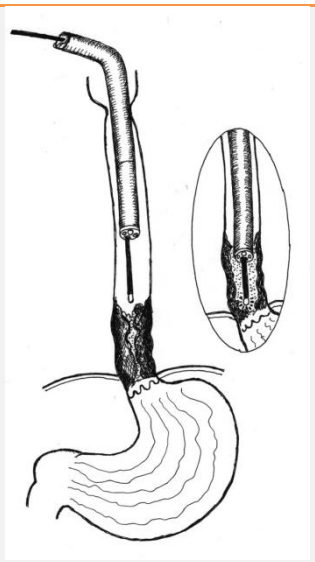
Scheme of the probe is shown in figure 2 A. Summary of minimally invasive interventions was as follows: Endoscopic diathermy tunneling (EDT) tumors in 17 (16.8%) and endoscopic stenting (ES) in 84 (83.2%). Endoscopic diatermotunelisation tumor performed in 17 (16.8%). Scheme of endoscopic diatermotunelisation is shown in figure 2 B. The reasons for rejection of stent placement was: in 14 cases, the absence of a circular growth suprastenotic expansion of the lumen of the distal esophagus, which can lead to migration of the implant, and in 3 patients, which was planned stenting, in step diatermotunelisation stepped perforation of the tumor, therefore the 2 patients operated on an emergency basis, and 1 patient was successfully conducted conservative treatment.

Table 2. Summary of therapeutic measures

Items	After exploratory surgery	Not operated patients	Total
Gastrostomy	3	-	3 (1.3%)
Symptomatic treatment	86	42	128 (55.2%)
Minimally invasive methods	21	80	101 (43.5%)
Total	110 (47.4%)	122 (52.6%)	232



A. Scheme of nasogastric tube feeding under the control of the endoscope



B. Scheme of endoscopic diathermy tunneling

Figure 2. Scheme of the probe

Endoscopic stenting

The basic meaning of the use of stenting (prolonged esophageal intubation) is the possibility of oral nutrition because tunneling and probing can not provide a long-term restoration of patency of the esophagus due to the constant growth of the tumor, occlusive lumen again. Thus, stent stenosis restricts tumor clearance, acting as a skeleton. However, stenting can not be used in all patients, as requires two conditions: the presence suprastenotic expansion and circular lesion to prevent stent migration. We used a stent made of silicone tube of his own design, developed in the endoscopy department of JSC "RSCS named after Acad. V.Vahidova". The stent is made individually from the silicone tube with a funnel-shaped initial part for preventing its migration. The required length and diameter were determined on the basis of endoscopic and radiologic data. Silicone stents: a straight and S-shaped, are presented in picture 1. We used 4 methods of endoscopic stenting:

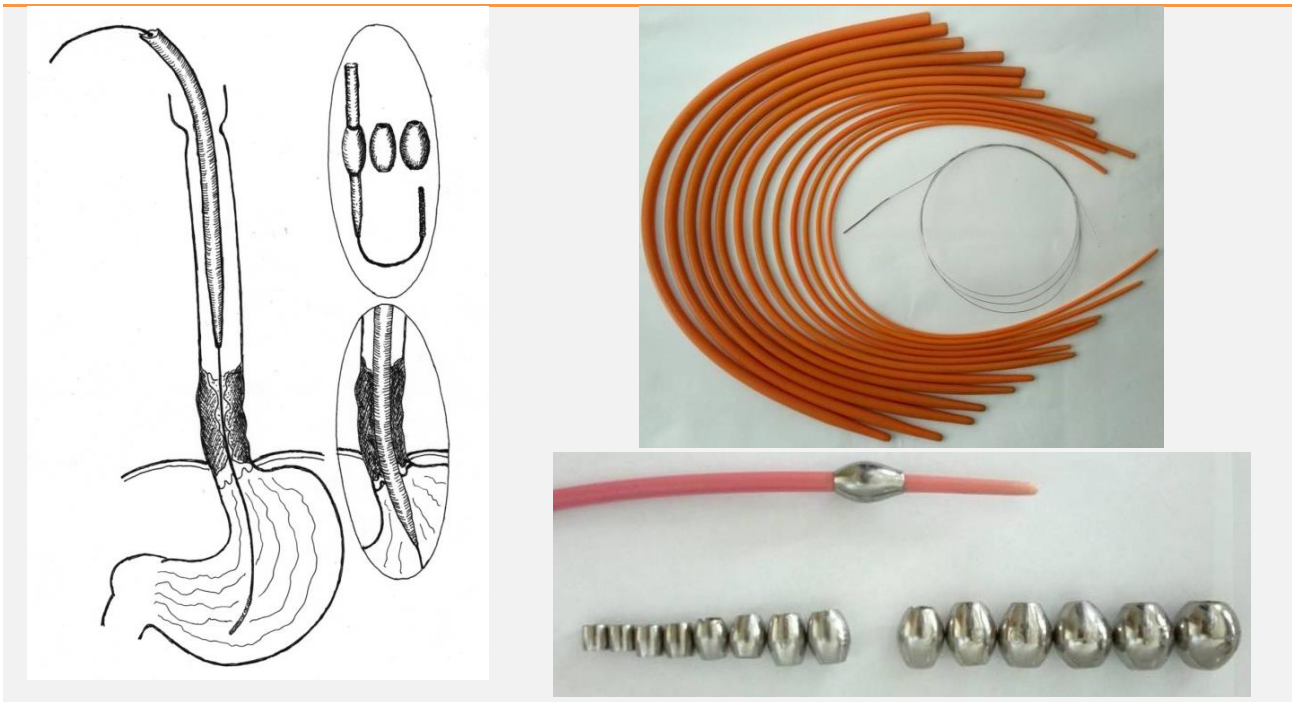
1. "Direct" when there is no need for pre-extension-rhenium luminal tumors performed in 11 (13.1%) cases;
2. Pre endoscopic diathermic tunalization tumor, described above, formed in 31 (36.9%) patients;
3. preliminary dilatation was performed in 15 (17.8%) patients;
4. preliminary endoscopic boujing (EB) performed in 27 (32.1%) patients.

It should be noted that the choice of method is individually endoscopic stenting and depends on the severity of the patient's condition, the nature of the tumor growth and the extent of its spread to the esophagus and stomach. If there is evidence to pre-expand the lumen of the tumor is currently prefer the combination of EDB and EB, which allow the most optimized and safely perform this manipulation. For the EB used a set of standard and interchangeable olive-proprietary. Scheme of endoscopic bougienage bougies and sets are shown in picture 2. Endoscopic stenting carried out under the supervision of endoscopy according to its own developed methods: the instrument on the endoscope and Bouje with the pusher tube. Scheme of endoscopic stenting is shown in figure 3.

All patients fulfilled the radiological control of the correct establishment of the endoprosthesis, which was carried out the next day after stenting. Of the 84 patients, 4 cases, which was 4.7%, the offset is set down endoprothesis, whereby the distal end of the prosthesis rested against the stomach wall. In this connection, the removal of the stent was performed followed by restenting. X-ray picture and scheme productions silicone stent is shown in picture 3.

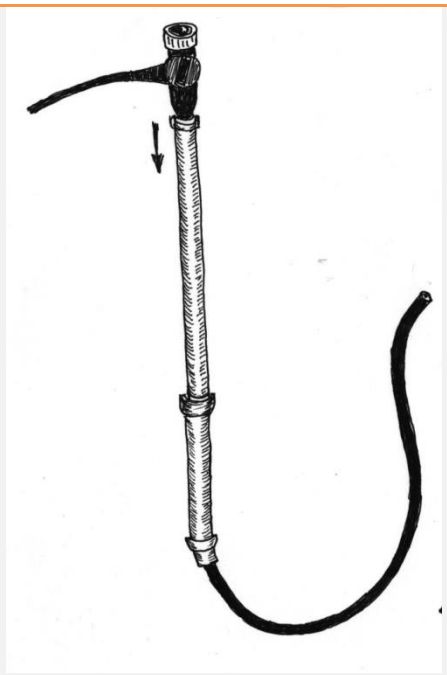
Straight stent S-shaped silicone stent

Picture 1. Type of stents

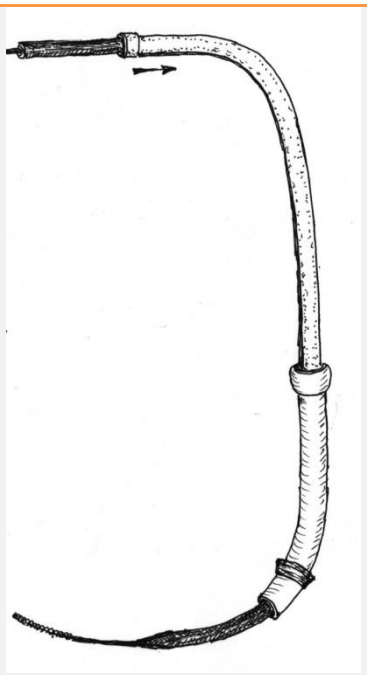


Scheme of endoscopic bougienage A set of traditional and removable bougies olive

Picture 2. Scheme of endoscopic bougienage

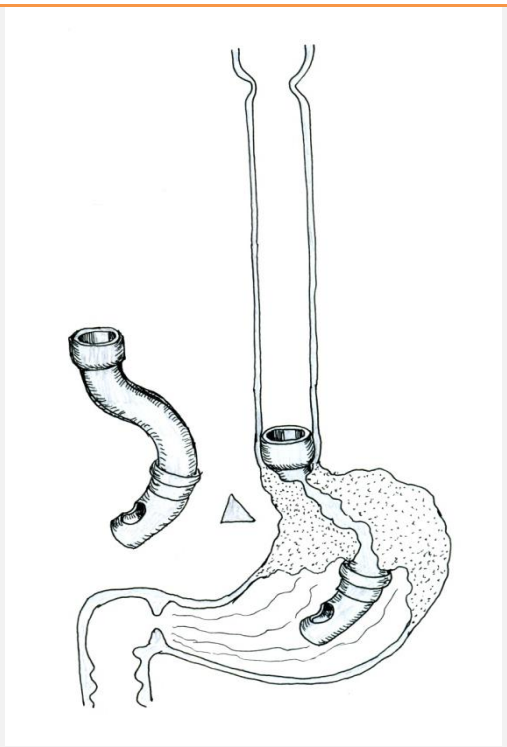


Stent in the device for endoscope

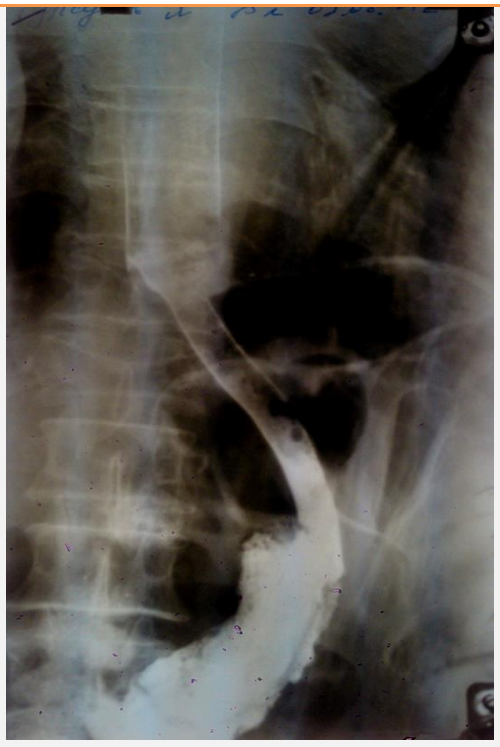


Stent in the bouje

Figure 3. Installation of stent and bouje



Scheme of installed S-shaped stent



X-Ray after installing endoprothesis

Picture 3. S-shaped stent

Despite its minimally invasive ES possible development of specific complications, which are divided into early and late complications:

A) Early complications. During the ES, observed track-guides complications: bleeding from the tumor area - 12 (11.8%); Function of the cardia of the stomach - 1 (0.99%); perforation of the abdominal department pi schevoda - 1 (0.99%); perforation of the lower third of the thoracic esophagus - 1 (0.99%). tumor perforation diagnosis was based on clinical data of objective examination and X-ray studies with water-soluble contrast. In this case, 1 case of laparotomy performed, suturing tumor defect, sanitation, drenaging and plugging with a satisfactory result. The remaining patients were discharged in a serious condition due to the ongoing

peritonitis and mediastinitis due to the categorical rejection of the proposed emergency operations. Bleeding in the form of vomiting fresh blood in all cases stopped by conservative measures.

B) Late complications. Among the specific complications inherent ES technique, the following were observed late complications: occlusion of the stent food - 18 (21.4%); obstruction of proximal part of the stent tumor - 9 (10.7%), occlusion of the distal stent tumor - 6 (7.1%); migration of the stent into the stomach - 3 (3.6%); migration of the stent in the esophagus - 1 (1.2%); pain, analgesics are not docked - 6 (7.1%). In cases of stent obstruction was conducted fragmentation food bolus under control endoscopy and push food at the distal end of the stent. When tumor obstruction of the proximal end of the stent held EDT followed by further restentirovaniem. In cases the tumor obstruction of the distal end of the stent was performed by only EDT. In cases of stent migration into the stomach was carried out under the supervision of the extraction of the stent endoscopy followed restenting. When the left-Bo syndrome, not cropped analgesics stent removed.

CONCLUSION

The introduction of endoscopic techniques has solved the most important issue - the elimination of dysphagia, which in these patients leads to nutritional depletion of non-resectable patients. Minimally invasive techniques described, the absence of a cosmetic defect, there is no need of specific care set endoprothesis and relatively easily tolerated by patients of the technique endoprothesis stent installation suggest a viable alternative to the imposition of gastrostomy and jejunostomy.

DECLARATIONS

Acknowledgements

This work was supported by "Republican Specialized Scientific and Practical Medical Center of Surgery named after Academician V.Vakhidov", Uzbekistan.

Authors' contributions

All authors contributed equally to this work.

Competing interests

The authors declare that they have no competing interests.

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2019 SCIENCELINE
Journal of Life Science and Biomedicine
J Life Sci Biomed, 9 (4): 89-95, 2019

ISSN 2251-9939

Effectiveness of stage by stage bariatric interventions for regression of comorbidity at obese class III patients

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ABSTRACT

Introduction. Currently obesity is considered as a chronic, relapsing, multifactorial neurobehavioral disease, in which an increase in body fat contributes to the dysfunction of adipose tissue and the biomechanical effect of adipose tissue on surrounding tissue with development of metabolic and psychosocial health effects. It has been proven that bariatric surgery significantly reduces the level of pro-inflammatory senility-associated secretory proteins (SASPs), weight reduction increases telomeres length and declines their oxidative degradation (lowering of oxidative stress in telomeres), miR10a_5p, which is post-regulated with increasing of biological age, decreased after surgery, what suggests that bariatric surgery abated the premature aging phenotype. It is of big interest to evaluate comorbidity conditions in people with obese class III after the intervention of intragastric balloons (IGB) and laparoscopic sleeve gastrectomy (LSG), which are lead to weight loss. Methods. A total of 40 patients (32 female and 8 male aged 19–55 years were considered for the study. Comorbidity was assessed by the structure and severity of diseases associated with obesity according to the recommendations of Nedogoda (2016). Cardiometabolic disease staging scale of Guo and Garvey (2015) was used to assess the metabolic health. Endovisual surgery-LSG was performed (n=40) on a laparoscopic set and instruments of Karl Storz, GMBH & CoKG (Germany). The spherical intragastric balloon (IGB) was installed according to the manufacturer's method (BIB ™ System Intragastric Balloon from Allergan Inc. USA) using a GIF-1T20 Olympus gastrointestinal fibroscope (Japan). Results. Evaluation of the obesity phenotype, a completely metabolically healthy phenotype was not detected in any case. Nowadays, the opinion about the usefulness of the clinical concept of the metabolic syndrome (MS) is disputed, because it has not been convincingly proven its predictive value exceeds that for individual components. Conclusion. Obese class III is associated with dyslipidemia/hypertriglyceridemia in 85%; with type 2 diabetes mellitus (DM2)/prediabetes in 50%; with arterial hypertension (AH) in 45%; and with non-alcoholic fatty liver disease (NAFLD) in 35% of cases. Therefore, two-stage treatment by IGB and LSG make it possible to improve the performance on the Cardiometabolic disease staging scale, achieving zero cardiometabolic risk in 35% of patients, and in rest of patients move to a lower stage.

Original Article

PII: S225199391900014-9

Rec. 18 May 2019
Rev. 30 June 2019
Pub. 25 July 2019

Keywords

Obesity,
Bariatric surgery,
Comorbidity,
Intragastric balloon,
Endovisual surgery.

INTRODUCTION

Currently, on the recommendation of the American Society for Metabolic & Bariatric Surgery Updates (2014-2015), obesity is considered as a "chronic, relapsing, multifactorial neurobehavioral disease, in which an increase in body fat contributes to the dysfunction of adipose tissue and the biomechanical effect of adipose tissue on surrounding tissue with development of metabolic and psychosocial health effects [1, 2]. The cost of medical care for people with obesity is significantly higher than for people with normal weight. So, for people with obese class I the cost of medical care is 14% more compared to those of normal weight, then for persons with obese class III - the cost is 77.1% more; comorbid pathology in obesity has a strong influence on these data [3].

Comorbidity - a combination of pathological conditions that worsen the patient's prognosis - the risk of death from competing diseases, the Charlson index allows to quantify this risk. According to a study that included 514,350 individuals [3], the Charlson Comorbidity Index (CCI) in non-obese individuals was 1.84; with overweight - 2.04; with obese class I - 2.29; class II - 2.7; class III - 3.06, respectively. The spectrum of CCI diseases includes ischemic heart disease, myocardial infarction, cerebrovascular diseases, peripheral vascular diseases, connective tissue diseases, chronic lung diseases, ulcers, chronic liver diseases, dementia, diabetes, hemiplegia, kidney diseases, tumors, leukemia, lymphoma, metastatic tumors, and immunodeficiency syndrome [4].

Diseases, traditionally associated with obesity, are arterial hypertension (AH), depression, type 2 diabetes mellitus (DM2), non-alcoholic fatty liver disease (NAFLD), sleep apnea [5-8]. Comorbidity with obesity also

includes a pro-inflammatory status, a phenotype of premature aging, including secretion of senility-associated secretory proteins (SASP) and telomere length reduction. Micro-RNA - non-coding molecules are able to modify the post-transcriptional processes causing a metabolically unhealthy condition [9].

It has been proven, that bariatric surgery significantly reduces the level of pro-inflammatory SASPs, weight reduction increases telomeres length and declines their oxidative degradation (lowering of oxidative stress in telomeres), miR10a_5p, which is post-regulated with increasing of biological age, decreased after surgery, what suggests that bariatric surgery abated the premature aging phenotype. Randomized trials have shown that excessive weight loss after laparoscopic sleeve gastrectomy (LSG) after 5 years is 61.1%; after shunting operations (Roux-en-Y bypass) - 68.3% (the differences are not significant), while the LSG is advantageous in terms of frequency of gastric reflux after surgery, showing 25%, whereas after shunting operations - 60.4%; the number of reoperations after LSG and shunting operations was 15.8% and 22.1%, respectively [10, 11]. According to Salminen et al. [12]'s data, in 5 years after LSG, weight loss was 49%, remission of DM2 and AH was achieved in 37% and 29% of cases, respectively, hypolipidemic therapy was stopped in 47% of patients.

Treatment with intragastric balloons (IGB) as a method of reducing excessive body mass, that does not require invasive surgery, has become widespread. The method is endoscopic, and opens up the possibilities of minimally invasive correction of obesity and serves as an alternative to diet therapy and medical preparation of patients for bariatric surgery [13]. The mechanisms of action of the IGB are can be explained as following: to decrease in the gastric reservoir due to the volume of the balloon, the achievement of early satiation during the meal, as well as slowing down the evacuation of food from the stomach.

Recent data suggests, that weight loss causes reduction of the risk of comorbidities, where the proportion of patients is 52-92% for AH, 82% - is for cardiovascular diseases (CVD) and bronchial asthma; 63% - is for dyslipidemia; in 82% of cases there is a decrease in the degree of hepatosis, in 20% - the degree of fibrosis in NAFLD is declined; 83% of patients achieved remission of DM2, in 95% patients lowered congestion in the venous vessels of the lower extremities; in 55% - depression is eliminated, and ultimately, in 95% of patients the quality of life is improved [14]. In consideration of above-given data, it is of interest to evaluate comorbid conditions in people with obese class III after the intervention of IGB and LSG, which are lead to weight loss.

MATERIAL AND METHODS

The objective of the research was 40 patients (32 female and 8 male) aged 19–55 years (34.7±2.5 years) hospitalized in the State Institution "Republic Specialized Scientific-Practical Medical Center of Surgery named after acad. V.Vahidov" in 2016-2019. All patients were obese class III. The class of obesity was assessed by WOG (2011), which provides for the Asian type. Criteria for Asians are next: lowered weight (<18.5 kg/m2), normal weight (18.5-22.99 kg/m2), overweight (23-24.99 kg/m2), obese class I (25-29.99 kg/m2), obese class II (30-34.99 kg/m2), obese class III (35-59.99 kg/m2) [15]. The metabolic unhealthy phenotype of obesity is considered to be an increase in waist circumference (WC) of more than 102 cm in male and 88cm in female, an increase in blood C-reactive protein (CRP) more than 3 mg/l; glucose - more than 5.6 mmol/l; triglycerides (TG) - more than 1.7 mmol/l; a decline in high-density lipoprotein (HDL) less than 1.04 in men and 1.30 mmol/l in women; elevation of blood pressure (BP) more than 130/85 mm Hg.

Comorbidity was assessed by the structure and severity of diseases associated with obesity according to the recommendations of Nedogoda [15]. Cardiometabolic Disease Staging scale [16] was used to assess the metabolic health [4]. Endovisual surgery - LSG was performed on a laparoscopic set and instruments of Karl Storz, GMBH & CoKG (Germany), using the Harmonic G11 ultrasonic scalpel (Johnson & Johnson, USA), Forse Triad energy platform with Liga Sure technology (USA), endoscopic stapling-transection devices of company Ethicon Endo Surgery (Johnson & Johnson, USA). This intervention is a restrictive bariatric surgical procedure. The technique of operation is consisted in resection most of the stomach, located along the greater curvature (curvature major) with preservation of the cardiac sphincter and pylorus and the formation of a narrow gastric tube with a volume of 60-150 ml, located along the lesser curvature (curvature minor). LSG was performed in 40 patients.

The spherical intragastric balloon (IGB) was installed according to the manufacturer's method (BIB ™ System Intragastric Balloon from Allergan Inc. USA) using a GIF-1T20 Olympus gastrointestinal fibroscope (Japan) under intravenous potentiation with the addition of a local anesthesia of pharynx with solution of Lidocaini 10% in spray. After filling the balloon with an adequate volume of liquid and removing the connecting tube-catheter, endoscopic monitoring of its position and hermetic properties was performed. The duration of

the IGB entire procedure was 10-15 minutes. The intervention was performed with the participation of an endoscopist, a surgeon, an anesthesiologist and an anesthesiological nurse. Patients were observed in 2-3 days, in order to prevent complications associated with the possible intolerance of patients to the presence of a balloon in the stomach. For the entire period of treatment, proton pump inhibitors (pantaprazole) were prescribed, which contributed to a decrease in gastric secretion. Removal of the balloon was carried out after 6 months.

C-reactive protein oncentration, serum lipid profile: total cholesterol (CH), triglycerides (TG), HDL, very low density lipoprotein cholesterol (VLDL), and glucose, uric acid (UA)), were determined on an automatic biochemical analyzer "VITROS-350" ("Ortho Clinical Diagnostics", USA). The atherogenic index (AI) was calculated using the Klimov's formula: AI = (cholesterol-HDL)/HDL.

Ethical approval

The review board and ethics committee of RSCS named after acad. V.Vakhidov approved the study protocol and informed consents were taken from all the participants.

RESULTS

We had divided all patients in 2 groups: the 1-st group consists of 34 patients with one stage treatment - only by LSG; the second group consists of 6 patients, which treated by IGB installation on 6 month (the 1-st step of treatment) and then LSG (the 2-nd step of treatment). Mean body mass index was 51.2±2.3 at the 1-st group and 62.2±1.3 kg/m2 at the 2-nd group patients. Evaluation of the obesity phenotype, a completely metabolically healthy phenotype was not detected in any case, since in all patients, waist circumference exceeded 88 cm in female and 102 cm in male. At the same time, 6 patients of the 1-st group had glucose levels below 5.6 mmol/l; at 5 patients of the 1-st group and 1 patient of the 2-nd group TG concentration was below 1.7 mmol/l; the level of HDL is over 1.3 in 5 women from 1-st group, blood pressure was lower than 130/85 at 18 patients (14 patients from 1-st group and 4 patients from 2-nd group). These data show the unequal occurrence of components of the metabolic syndrome (MS) in obese people.

Table 1. Diseases associated with obesity and their stages 6 months after LSG (by Nedogoda scale)

Items \ Diseases	Stage 0 (absent)	Stage 1	Stage 2	stage 0 (absent)	Stage 1	Stage 2
	Before LSG			After LSG		
DM2/prediabetes	20 (50%)	18(45%)	2(5%)	30(75%)	6(15%)	4(10%)
AH	22(55%)	-	18(45%)	34(85%)	2(5%)	4(10%)
hypertriglyceridemia/dyslipidemia	6(15%)	26(65%)	8(20%)	22(55%)	12(30%)	6(15%)
Sleep apnea syndrome	40(100%)	-	-	40(100%)	-	-
NAFLD	26(65%)	14(35%)	-	32(80%)	8(20%)	-
Polycystic ovaries syndrome	40(100%)	-	-	40(100%)	-	-
Fibrillation of atrium	40(100%)	-	-	40(100%)	-	-
Osteoarthritis	40(100%)	-	-	40(100%)	-	-
GERD	38(95%)	2(5%)	-	38(95%)	2(5%)	-
Hypodinamic lifestyle	-	28(70%)	12(30%)	26(65%)	8(20%)	6(15%)
Depression	30(75%)	10(25%)	-	38(95%)	2(5%)	-

AH= arterial hypertension, DM2= type 2 diabetes mellitus, NAFLD=non-alcoholic fatty liver disease, GERD= gastroesophageal reflux disease, LSG= laparoscopic sleeve gastrectomy.

Nowadays, the opinion about the usefulness of the clinical concept of the MS is disputed, because it has not been convincingly proven its predictive value exceeds that for individual components; it could be more informative to indicate everyone component separate, moreover, since all the criteria for diagnosing MS suggest the presence of three components, and, in fact, we are talking about various options for combining obesity with elevated blood pressure, dyslipidemia, hypertriglyceridemia, and impaired glucose tolerance [14, 16, 17]. Evaluation of diseases, associated with obesity, at patients of 2-nd group (n=6) showed that AH (stage 2 according Nedogoda scale) was found at 4 patients; hypertriglyceridemia/dyslipidemia, at 5 patients (at 2 patients - the stage 2, at 3 patients, the stage 1 according Nedogoda scale); at 3 patients was prediabetes (1-stage according Nedogoda scale), at 5 patients – depression. All patients of the 2-nd group had high anestesiological risk, LSG was contraindicated for them. So, IGB was installed to these patients. It was very effective to weight

loss and cardiometabolic risk reduction. After 6 month IGB was removed with good result: body mass index (BMI) reduced from 62.2±1.3 kg/m2 to 50.1-52.4 kg/m2, hypertriglyceridemia/dyslipidemia reduced at 5 patients to stage 0; AH reduced at 4 patients (to stage 1 at 3 patients and to stage 0 at 1 patient); at 2 patients fasting glucose level became normal (stage 0); at 4 patients reduced depression (stage 0). After IGB removing patients of the 2nd group were underwent LSG (2-nd step of treatment).

For evaluation effectiveness of LSG we have united patients of the 1-st and the 2-nd groups (n=40). Evaluation of comorbidity before LSG showed that AH was the most frequent, at 18 patients (45%), NAFLD 1-2 degree was 14 (35%). In addition, in 11 (28%) cases cholecystitis was found without stones, gastritis was in 5 (13%) cases, goiter in 6 (15%), and ventral herniain 1 (3%) case, Ischemic heart disease (IHD) and DM2 was in 1 patient (3%). After LSG, there was a significant decrease in the number of patients with DM2/prediabetes, AH, hypertriglyceridemia/dyslipidemia (Table 1).

DISCUSSION

Discussion of this data confirms that our results reflects common trend. So, according to Song et al. [3], obesity strongly increases the risk of developing hypertension (RR = 2.33); complicated DM2 (RR=2.22); uncomplicated DM2 (RR=1.85); IHD (RR=1.58); chronic liver disease (RR = 1.3); cerebrovascular diseases (RR=1.08); meanwhile, the overall risk for all diseases in people with BMI over 30 kg/m2 is quite high (RR = 2.22) [3].

It is known, that the class of obesity greatly influences the growth of comorbidity of AH, DM2 and chronic liver diseases; whereas the incidence of Ischemic heart disease (IHD), cerebrovascular diseases, depression does not increase significantly depending on the increase in BMI, being approximately less than 8-10% in normal-weight and 10-15% in people with obese class III, while the incidence of AH in people with normal weight/overweight is about the same and is about 18%, and in persons with obese class III - more than 50%; chronic liver diseases in overweight people occur in 18%, and in obese class III - in 35% of cases, for DM2, these numbers are 16-18% in overweight and 45% in obese class III [4].

Of particular interest is NAFLD — a systemic disorder, which associated with various chronic conditions, including obesity, diabetes, kidney disease, and cardiovascular diseases [15]; some authors supposed that NAFLD – is a hepatic manifestation of the MS [18]. The frequency of NAFLD has increased over the past 30 years in direct correlation with an increase in sugar consumption (sugar-containing beverages, cakes) and the development of obesity [19]. Liver lipogenesis is an insulin and glucose-dependent process that is controlled by transcription factors. At the presence of insulin resistance (IR), the formation of lipids from glucose in the liver is enhanced by the transcription factor SREBP-1c, and its targets are the enzymes of the synthesis of fatty acids (FA) – palmitoil-synthase, acetyl-CoA-carboxylase, stearoyl-CoA desaturase [20].

Our results indicate a significant regression of diseases associated with obesity, as well as a reduction in the factors responsible for the metabolic unhealthy phenotype of obesity. In addition, there was a positive dynamics of a significant decrease in the level of UA from 359±18 to 283±9 μmol/l (the difference with the initial data was 21.2%, $P<0.05$) and the CRP from 15.5±0.2 to 5.0±0.5 mg/l (the difference with the initial data - 66.7%, $P<0.05$).

Discussing the pathogenetic role of UA in obesity, we note that UA has a pro-inflammatory effect and enhances lipogenesis, and is closely associated with the development of NAFLD [21]. The pro-inflammatory effect of UA is realized through the activation of NFkB, stimulation of NLRP3 by inflammosomas, activation of NADPH-mitochondrial (MCH) oxidase, which increases the accumulation of reactive oxygen species (ROS). It is known that two enzymes are sensitive to ROS in mitochondria — enoyl-CoA hydratase (an enzyme of fatty acid beta-oxidation) and aconitase — an enzyme of the Krebs cycle [22]. Oxidative modification of aconitase and enoyl-CoA hydratase leads to their inactivation, resulting in an increase in citrate, its release into the cytosol and increased lipogenesis. Synthesis of UA is associated with generation of ROS, which initiate oxidative stress (OS) both in mitochondria and in the endoplasmic reticulum (EPR), inducing inflammation and fibrosis, as well as insulin resistance. OS in MCH and EPR of hepatocytes lead to activation of the sterol-regulatory element that binds the transcription factor beta (SREBP-1c), followed by stimulation of lipogenesis through the activation of acetyl-Coa-carboxylase [22, 23]. Clinical studies have shown that the degree of liver fibrosis according to biopsy is higher in patients with high concentration of UA [12]. Meta-analysis confirmed that the frequency of NAFLD increases by 3% with an increase in UA by 1 mg/dL [20]. It is possible, that the decrease in UA levels that we detected in our patients also contributes to the regression of comorbidity in the bariatric treatment of obesity.

In the majority of clinical recommendations, a good target effect from the point of health is considered to be a weight reduction of 3-10% within 6 months and its subsequent stabilization. With a BMI of more than 35

kg/m2 and the presence of comorbid pathology, a weight reduction target is of more than 10%, and with a BMI of ≥ 40 kg/m2 by 20-25% (AACE/ACE, 2014) [1]. As our results, after limiting the amount of ingested food by reducing the volume of the stomach after IGB installation weight loss was 17.7%, after LSG – 19.5% from the baseline, respectively. At the patients of the 2-nd group after 2 steps of treatment (IGB installation and LSG) weight loss was 33.8% from baseline level. IGB was established for 6 months as a preoperative preparation to reduce perioperative risk, followed by LSG. Improving the metabolic profile in patients after treatment reflects the average numbers of anthropometry and laboratory tests (Table 2).

Table 2. Characteristics of lipid profile, pro-inflammation cytokines 6 month after LSG

Patients group	Control group, n=10	Before LSG, n=40	After LSG (6 month), n=40
WC, cm	76±1.0	130.6±2.5*	120.3 ±2.1*,**
BMI, kg/m^2	23.4±0.3	51.2±2.3*	41.2±1.4**
Fasting glucose, mmol/l	4.7±0.1	6.05±0.21*	5.58±0.04*,**
TG, mmol/l	0.93±0.05	1.56±0.18*	0.99±0.11**
VLDL, mmol/l	0.44±0.11	1.14±0.06*	0.61±0.13**
CH, mmol/l	4.4±0.1	5.1±0.3*	4.07±0.26**
HDL, mmol/l	1.34±0.03	0.99±0.05*	1.07±0.06*,**
Atherogenic index	2.3±0.2	4.2±0.2*	2.8±0.1*,**

Note: * - significant relative to control, p <0.05; ** - significant relative to baseline characteristics. LSG= laparoscopic sleeve gastrectomy, WC=waist circumference, BMI=body mass index, CH=total cholesterol, TG=triglycerides, VLDL=very low density lipoprotein cholesterol, HDL=high-density lipoprotein,

In patients after LSG the lipid profile, fasting glucose level did not differ significantly from the control group (P>0.05), indicating that LSG is effective in the first 6 months after the intervention. When choosing the method of operation of patients with obese class III, such factors as BMI, cardiopulmonary diseases and other factors that increase the risk of abdominal operations come to the fore. IGB can be effectively used as a preoperative preparation in individuals with extremely high body mass as the first stage of weight loss before LSG.

Regarding the results, we note that, according to randomized trials, caloric restriction of food allows achieving sustainable weight loss, and even with subsequent weight gain, the positive effect of weight loss on pro-inflammatory markers and biochemical parameters persists permanently [24]. According to Shelest et al. [23], it is obesity that makes a significant contribution to the increase in pro-inflammatory cytokines and adipocytokines. These authors have shown that in patients with AH in combination with obesity, there was a significant increase in leptin and decrease in adiponectin on the background of a significant increase in IL-6 and IL-10; in hypertension without obesity, these parameters did not change significantly relative to control (P>0.05) [25]. As our observation study showed, all patients after bariatric intervention have improved metabolic health, assessment with Cardiometabolic Disease Staging scale by Guo and Garvey [16] showed that zero (0) stage, when there are no risk factors, was observed in 14 (35%) patients (before treatment - none); Stage 1 (2 risk factors) - in 20 (50%) patients versus 18 before treatment; Stage 2 (3 or more risk factors) - in 4 patients versus 8 before treatment; Stage 3 (3 factors + prediabetes) - in 4 versus 12 before treatment; Stage 4 (DM2, CHD, etc.) - in 2 patients (Figure 1).

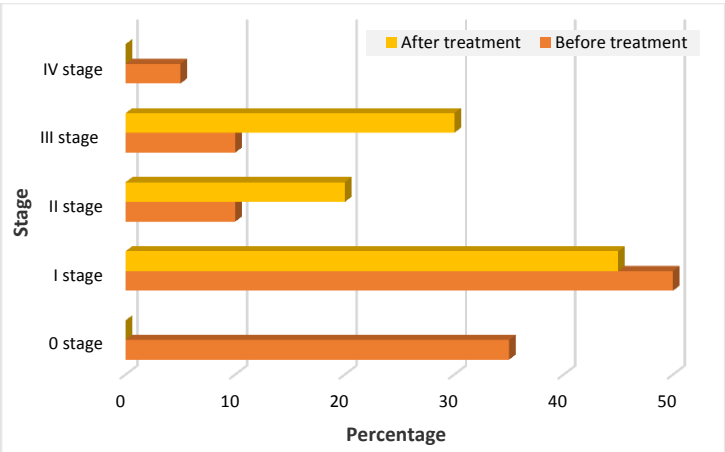

Figure 1. Regression of cardiometabolic risk stages in the dynamics of bariatric treatment (% of patients).

CONCLUSION

Obese class III is associated with dyslipidemia/hypertriglyceridemia in 85%; with DM2/prediabetes - in 50%, with AH in - 45%; and with NAFLD - in 35% of cases. IGB as the 1-st step of treatment allow to achieve a reduction in BMI by on 17,7% of the baseline, and regression of comorbidity. Two step treatment – IGB and then LSG caused reduction of weight on 33,8% in 12 month after starting of treatment. LSG caused reduction of comorbidity: prediabetes decreases by 2 times, AH - by 3 times; dyslipidemia – 1,9 times; reduction of NAFLD – 1,8 times in 6 months after the intervention. Two stage treatment by IGB and LSG make it possible to improve the performance on the Cardiometabolic Disease Staging scale, achieving zero cardiometabolic risk in 35% of patients, and in rest of patients - move to a lower stage. Reduction in weight and comorbidity because of LSG and IGB combined with a significant reduction in UA and SRP.

DECLARATIONS

Acknowledgements

This work was supported by "Republican Specialized Scientific and Practical Medical Center of Surgery named after Academician V.Vakhidov", Uzbekistan.

Authors' contributions

All authors contributed equally to this work.

Competing interests

The authors declare that they have no competing interests.

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2019 SCIENCELINE
Journal of Life Science and Biomedicine
J Life Sci Biomed, 9 (4): 96-101, 2019

ISSN 2251-9939

Characteristics and early clinical outcomes of patients undergoing living-related kidney transplantation

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ABSTRACT

Aim. This study aimed to access early outcomes of living-related kidney transplantation. Methods. The results of treatment of 159 patients (135 males and 24 females) with chronic renal disease during 2010-2018, have been investigated. Two new and traditional methods have been studied. New optimized method was performed for the main group (n=98) observed since February 2018, while the comparison group (n=61) from 2010 to February 2018 was operated in the traditional way. The characteristics of the patients were compared using the Wilcoxon rank-sum test or the Fisher's exact test as appropriate. All tests were two-sided, and P<0.05 was considered statistically significant. Analyses were performed using the R statistical package. Results. In 149 (93.7%) cases, the functional activity of the kidney transplants was assessed as a primary functioning graft with 95 (96.9%) cases in the main group and 54 (88.5%) in comparison group (P=0.048). Delayed graft function was detected in 2 (2.0%) recipients of the main group and in 5 (8.2%) cases of the comparison group. In the postoperative period, a significant decrease in creatinine level was observed in the main group of recipients and on the 1st day it was 221.0±58.7μmol/L, whereas in the comparison group the index was 569.3±84.6 μmol/L (P<0.001). 3-4 days after surgery, the level of blood creatinine in the main group was significantly (P<0.01) lower than the comparison group (149.6±25.6 vs. 343.6±69.4 μmol/L). On the first day after surgery, there was also a significant decrease (P<0.05) in urea level of the main group (11.4±1.61 mmol/L) in comparison with the comparative group (15.4±0.84 mmol/L). At the time of hospital discharge of recipients, the level of urea was within normal limits and equal to 8.3±0.80 mmol/L and 9.0±0.95 mmol/L in the main and comparison groups, respectively (P>0.05). Hemodialysis was required in 3 (3.1%) recipients from the main group and 3 (4.9%) from the comparison group. The need for corticosteroid therapy was observed in 2 (2.0%) cases of the main group and in 3 (4.9%) cases from the comparison group. Conclusion. The effectiveness of improved approaches to patient management and surgical tactics of related kidney transplantation has been proved, taking into account the verification of the graft functional activity on the main clinical and biochemical data of the terminal stage of chronic renal failure regression.

Original Article

PII: S225199391900015-9

Rec. 06 June 2019
Rev. 15 July 2019
Pub. 25 July 2019

Keywords

Kidney Transplantation, Living-Related Renal Transplant Recipients, Early Clinical Outcomes

INTRODUCTION

Kidney transplantation is the treatment of choice for chronic kidney disease. The risk of death for kidney transplant recipients (KTRs) is less than half of that for dialysis patient. Any differences in patient survival attributable to different immunosuppressive medication regimens are substantially smaller than the survival difference between dialysis and transplantation. Specifically, marginally inferior immunosuppressive medication regimens will result in substantially better patient outcomes than dialysis. Thus, it is better to perform kidney transplantation even with an inferior immunosuppressive regimen, than to avoid transplantation altogether [1].

According to the world medical statistics, organ transplantation of living donors has a lower incidence of graft rejection, as well as more satisfactory patient survival rates [2, 3, 4]. Currently, there is an improvement in kidney transplantation results, in connection with which more and more patients with end-stage renal disease prefer kidney transplantation to permanent program dialysis [5, 6].

Every year around the world, the number of living kidney donors increases. It is also likely that laparoscopic donor nephrectomy, which has a shorter duration of disability and fewer days of hospitalization, will further increase the number of living donors [7, 8].

In the conditions of the national health care system, kidney transplantation, as a radical form of treatment of chronic renal insufficiency, is at the stage of active development. In this connection, the aim of study was assessment early outcomes of living-related kidney transplantation.

MATERIAL AND METHODS

The results of treatment of 159 patients (135 males and 24 females) with chronic renal disease, which were observed from 2010 to 2018 in the department of vascular surgery and kidney transplantation of "RSSPMCS named after academician V. Vakhidov" were used as the main material. In the course of the research, modern principles of diagnosis and treatment were used, and complaints, objective examination data, laboratory and instrumental studies, immediate and long-term results of related kidney transplantation were also analyzed. The main group consisted of 98 cases observed since February 2018, in which kidney transplantation was performed according to a new optimized method, the comparison group included 61 cases from January 2010 to February 2018 operated in the traditional way. Among the recipients of both groups, patients aged from 20 to 44 years prevailed. In the majority of cases, surgeries were performed for male recipients - 135 (84.9%) cases. The main cause (95.6%) of renal failure was chronic glomerulonephritis, chronic pyelonephritis was detected in 1 (0.6%) case, 1 recipient (0.6%) suffered from type I diabetes, in 2 (1.2%) of the cases had urolithiasis, in 1 (0.6%) of the patient - chronic renal disease of unknown etiology, and in 1 (0.6%) of the cases polycystic kidney disease was detected.

Statistical analyze

The characteristics of the patients were compared using the Wilcoxon rank-sum test or the Fisher's exact test as appropriate. All tests were two-sided, and $P<0.05$ was considered statistically significant. Analyses were performed using the R statistical package.

Ethical approval

The review board and ethics committee of RSCS named after acad. V.Vakhidov approved the study protocol and informed consents were taken from all the participants.

RESULTS AND DISCUSSION

Despite modern advances in immunosuppression and immunological selection, the results of a living-related kidney transplantation are better than the results of a cadaveric kidney transplant both in the early periods after surgery and in the long-term period [9, 10]. Literature data allow us to conclude that organ transplantation from a living-related donor is acceptable from a clinical and ethical perspective and turns out to be the most effective method of treating patients. In most cases, family members of the patient are living donors, but recently there has been an increase in the number of donors who have no genetic relationship with the patient (friends, relatives) [6, 8].

In our study by analyzing the results of living-related kidney transplantation from the early postoperative period, it was revealed that during the study period from 2010 to February 2018 (comparison group) a relatively high frequency of complications was recorded.

Table 1. Complications of immediate post-operative period

Type of complication	Main group		Comparison group		All	
	Abs.	%	Abs.	%	Abs.	%
Subcutaneous hematoma	1	1,0%	1	1,6%	2	1,3%
Subcutaneous seroma	0	0,0%	2	3,3%	2	1,3%
Lymphorrhea	2	2,0%	2	3,3%	4	2,5%
Hematoma in the graft bed	3	3,1%	5	8,2%	8	5,0%
Wound suppuration	1	1,0%	1	1,6%	2	1,3%
Deep wound infection	0	0,0%	1	1,6%	1	0,6%
Failure of ureterocystanastomosis	0	0,0%	1	1,6%	1	0,6%
Bronchopulmonary complications	4	4,1%	4	6,6%	8	5,0%
Acute cardiovascular failure with a functioning transplant	2	2,0%	3	4,9%	5	3,1%

Table 1 reflects the complications observed in the early post-op period in the group of renal transplant recipients. Thus, a hematoma in the transplant bed developed in 3 (3.1%) patients of the main group and in 5 (8.2%) cases of the comparison group, making 5.0% of the total number of kidney transplant surgeries. Also, among the significant complications, bronchopulmonary complications can be identified with the development of acute respiratory failure, which were recorded in 8 (5.0%) cases, in 4 (4.1%) cases among recipients of the main group and in 4 (6,6 %) - comparison group. In the main group of recipients 2 (2.0%) cases of acute cardiovascular insufficiency were noted, in the comparison group it was 3 (4.9%) cases.

In 149 (93.7%) cases, the functional activity of the kidney transplants was assessed as a primary functioning graft (Table 2), with 95 (96.9%) cases in the main group versus the comparison group (54 (88.5%); p=0.048). Delayed graft function was detected in 2 (2.0%) recipients of the main group and in 5 (8.2%) cases of the comparison group.

Table 2. Graft functional activity

Items	Main group		Comparison group		All	
	Abs.	%	Abs.	%	Abs.	%
Primary functioning graft	95	96,9%	54	88,5%	149	93,7%
	χ^2 test =3,916; Df=1; p=0,048				-	-
Delayed graft function	2	2,0%	5	8,2%	7	4,4%
Acute Graft Rejection	1	1,0%	2	3,3%	3	1,9%
Total	98	100,0%	61	100,0%	159	100,0%

Acute graft rejection was observed after 3 (1.9%) surgeries, while 2 (3.3%) cases were in recipients of the comparison group. In order to assess the kidney transplant function, we studied the dynamics of creatinine (μmol/L) and urea indices in recipients.

Figure 1 showed that the differences in baseline creatinine values in the studied groups were not statistically significant (P>0.05) and amounted to 883.2±24.6 and 923.4±36.0 μmol/L in the main and comparison groups, respectively. In the postoperative period, a significant decrease in creatinine level was observed in the main group of recipients and on the 1st day it was 221.0±58.7 μmol/L, whereas in the comparison group the index was 569.3±84.6 μmol/L (P<0.001). 3-4 days after surgery, the level of blood creatinine in the main group was 149.6±25.6 μmol/L, significantly lower than the comparison group (343.6±69.4; P<0.01).

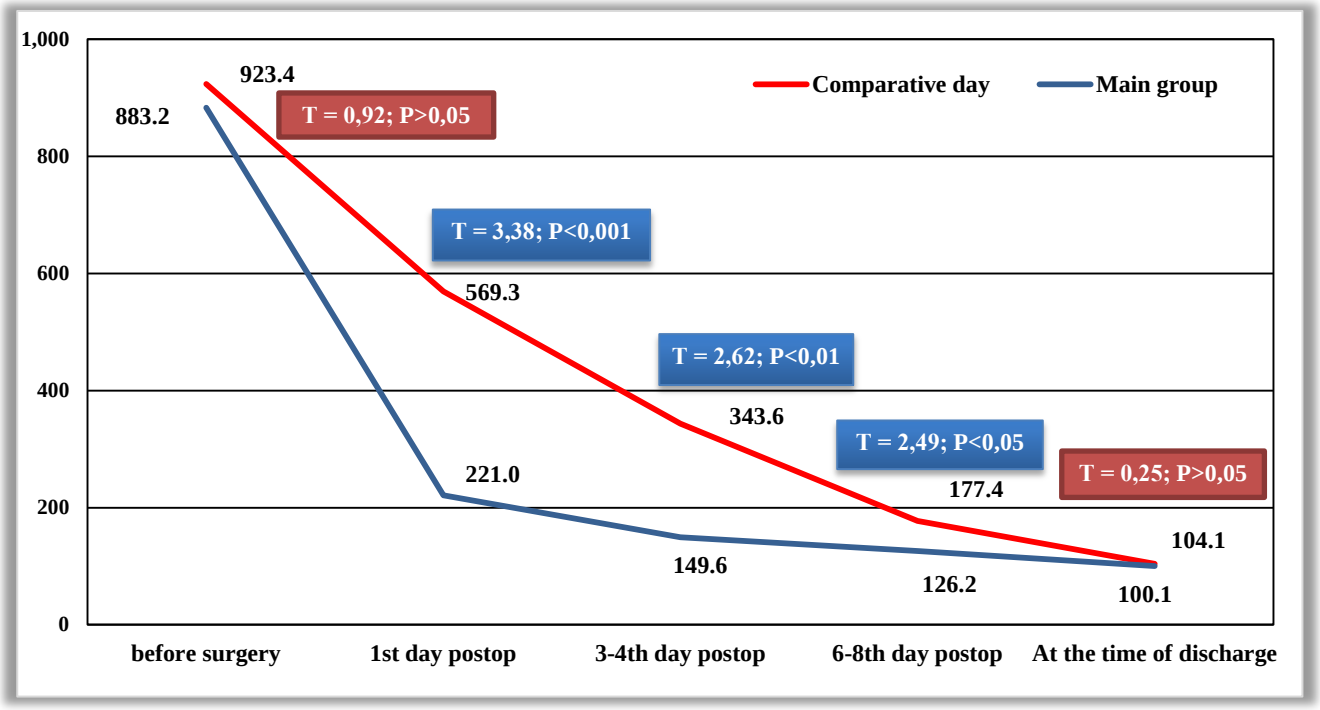

Figure 1. Dynamics of creatinine (μmol/L) after a related kidney transplant

It was also of interest to analyze the dynamics of urea indicators after living-related kidney transplantation, which is shown in figure 2. Thus, it can be noted that the differences in baseline values in the studied groups were not statistically significant (P>0.05) and amounted to 24.8±0.87 and 26.0±1.13 μmol/L in the main and comparison groups, respectively. From the presented dynamics, it can be seen that on the first day after surgery there was a decrease in urea levels to 11.4±1.61 mmol/L for the main group and to 15.4±0.84 mmol/L for the comparison group (P<0.05). At the time of discharge of recipients from the hospital, the level of urea was within normal limits and equal to 8.3±0.80 mmol/L and 9.0±0.95 mmol/L in the main and comparison groups, respectively (P>0.05).

Glomerular Filtration Rate (GFR), as one of the main indicator of kidney transplant function, was also evaluated by in the dynamics of the postoperative period. A graphical representation of the dynamics of changes in the GFR calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula is shown in Figure 3.

In the main group significantly better GFR values were observed already on the 1st day after surgery relative to the comparison group and averaged 67.5±2.97 ml/min (P<0.01). At the time of discharge, the GFR was equal to 95.4±2.63 and 88.9±3.94 ml/min in the main and comparison groups, respectively (P>0.05).

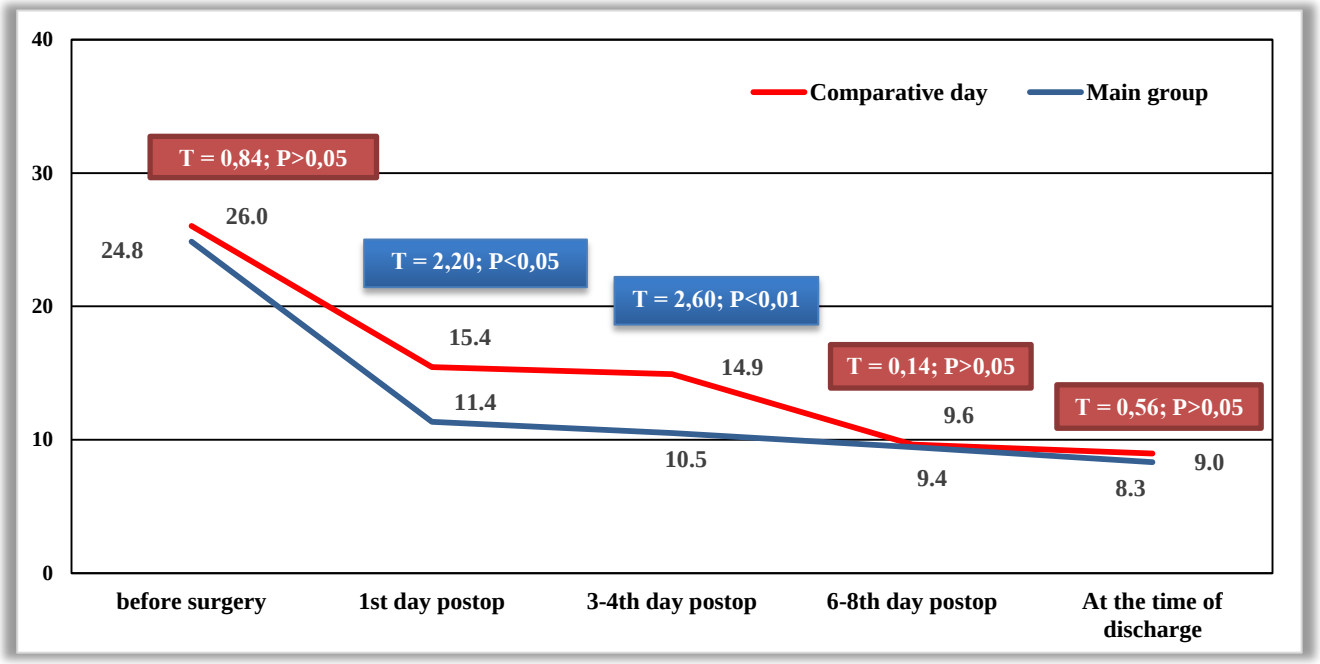

Figure 2. Dynamics of urea (mmol/L) after living-related renal transplantation

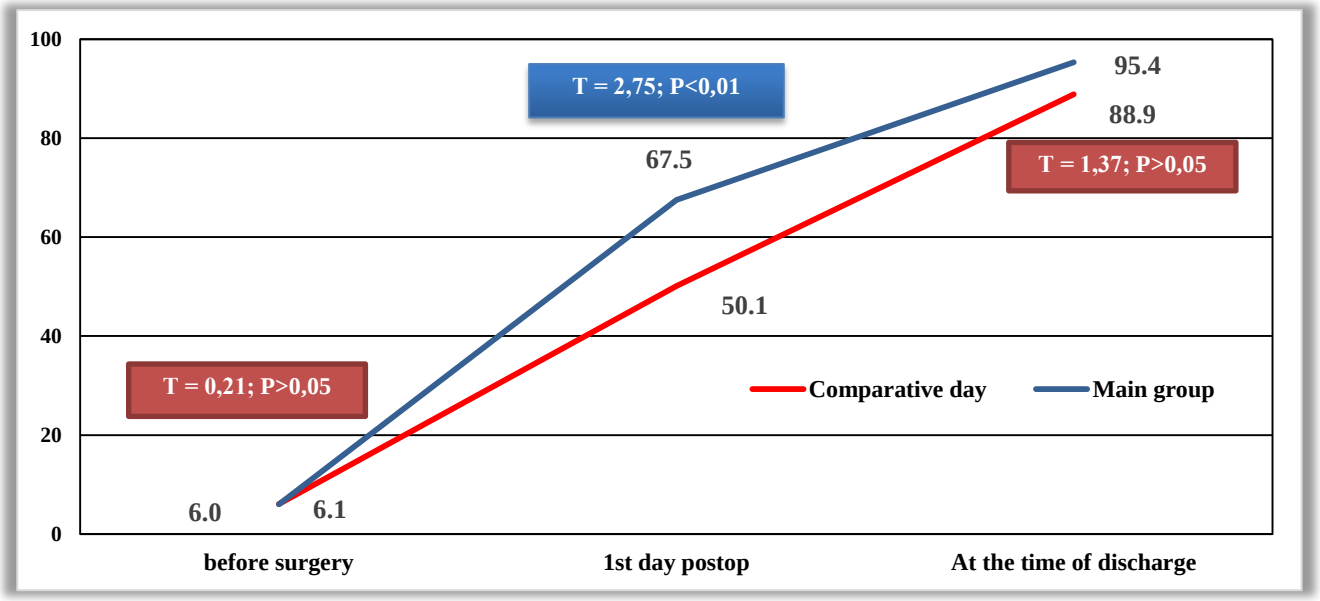

Figure 3. Dynamics of GFR (CKD-EPI) (ml / min) after related renal transplantation

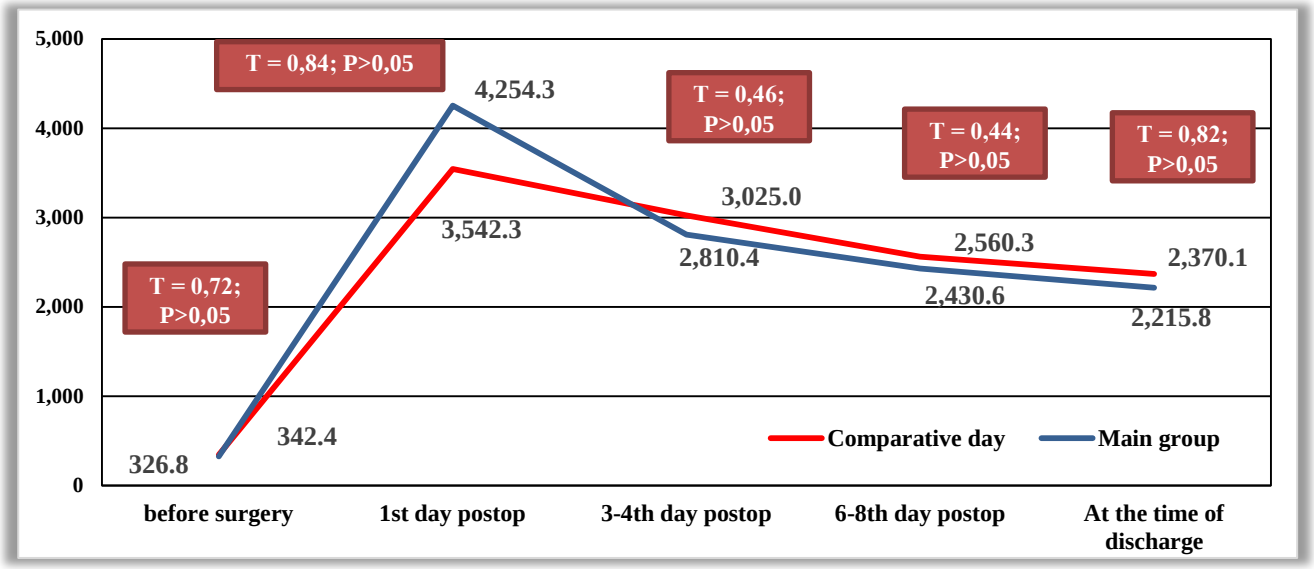

Figure 4. Dynamics of daily diuresis (ml)

When analyzing the indices of daily diuresis in the studied groups of recipients, positive dynamics was revealed in the main and comparison groups without significant difference. So, on the 1st day after surgery, the daily output increased from 326.8±16.3 ml to 4254.4±318.9 ml in the main group and from 342.4±14.2 ml to 3542.3±567.4 ml in the comparison group (P>0.05). By the time of the discharge of the recipients, the daily diuresis was 2215.8±129.5 ml and 2370.1±136.1 ml in the main and comparison groups, respectively (Figure 4).

Data of times of creatinine normalization in the studied groups are reflected in table 3. Thus, in 137 (86.2%) of the total number of patients, creatinine normalization lasted up to 5 days in the postoperative period, 88 (89.8%) and 49 (80.3%) recipients from the main and comparison groups, respectively. On days 6-7 after surgery, normal creatinine values were 2 (2.0%) recipients from the main group and 2 (3.3%) from the comparison group. In 4 (2.5%) cases out of the total number studied, it took 10 or more days to normalize creatinine.

Hemodialysis was required in 3 (3.1%) recipients from the main group and 3 (4.9%) from the comparison group. The need for corticosteroid therapy was observed in 2 (2.0%) cases of the main group and in 3 (4.9%) cases from the comparison group (Table 3).

Table 3. The timing of the normalization of creatinine

Items	Main group		Comparison group		All	
	Abs.	%	Abs.	%	Abs.	%
Up to 5 days	88	89,8%	49	80,3%	137	86,2%
6-7 days	2	2,0%	2	3,3%	4	2,5%
8-9 days	1	1,0%	2	3,3%	3	1,9%
10 or more days	2	2,0%	2	3,3%	4	2,5%
Hemodialysis was required	3	3,1%	3	4,9%	6	3,8%
It took a pulsotherapy	2	2,0%	3	4,9%	5	3,1%

CONCLUSION

The development of a national school of living-related kidney transplantation made it possible to achieve an earlier normalization of the main clinical and biochemical parameters (P<0.05-0.001) and thereby improve the early postoperative indicators of normal functional activity of the graft at the time of discharge from 90.2% (in the comparison group) to 94.9% (in the main group).

DECLARATIONS

Acknowledgements

This work was supported by Republican specialized scientific–practical medical center of surgery named after academician V.Vakhidov, Tashkent, Uzbekistan

Authors' contributions

All authors contributed equally to this work.

Competing interests

The authors declare that they have no competing interests.

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2019 SCIENCELINE
Journal of Life Science and Biomedicine
J Life Sci Biomed, 9 (4): 102-108, 2019

ISSN 2251-9939

Review on: regenerative medicine, tissue engineering and stem cell therapy in diabetes mellitus

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ABSTRACT

Introduction. In view of the recent success in pancreatic islet transplantation, interest in treating diabetes by the delivery of insulin-producing β-cells has been renewed. Because differentiated pancreatic β-cells cannot be expanded significantly in vitro, β-cell stem or progenitor cells are seen as a potential source for the preparation of transplantable insulin-producing tissue. In addition to embryonic stem (ES) cells, several potential adult islet/β-cell progenitors, derived from pancreas, liver, and bone marrow, are being studied. To date, none of the candidate cells has been fully characterized or is clinically applicable, but pancreatic physiology makes the existence of one or more types of adult islet stem cells very likely. It also seems possible that pluripotential stem cells, derived from the bone marrow, contribute to adult islet neogenesis. Aim. In future studies, more stringent criteria should be met to clonally define adult islet/β-cell progenitor cells. If this can be achieved, the utilization of these cells for the generation of insulin-producing β-cells in vitro seems to be feasible in the near future. This review will focus on the potential of adult tissue-derived stem cells, in lieu of embryo-derived stem cells, for the treatment of diabetes. We discuss the role of adult islet stem/progenitor cells in normal physiology, highlight possible candidate cells isolated to date, and describe different approaches for stem cell-based therapy.

Review Article

PII: S225199391900016-9

Rec. 06 June 2019
Rev. 15 July 2019
Pub. 25 July 2019

Keywords
Embryonic Stem Cells, Insulin-Producing, Pancreatic Islet, Physiology, β-cells

INTRODUCTION

Diabetes is a syndrome characterized by an absolute or relative β-cell deficiency in terms of mass (type 1 diabetes mellitus, T1DM) [1]. In contrast, in type 2 diabetes (T2DM) insulin deficiency, while, due in part to loss of functional, responsive β-cells, is not absolute, but relative to the impaired insulin signalling present in this disorder [2], or pancreas is unable to produce insulin, whereas type 2 (adult onset diabetes) is caused due to insulin resistance of the cells [3].

Once insulin resistance develops in several tissues, insulin-stimulated glucose disposal is decreased and adipocytes release many free fatty acids (FFAs). Furthermore, increased FFAs inhibit the insulin action on liver, resulting in increased gluconeogenesis in the hyperglycemic state [4]. The International Diabetes Federation estimates that up to 95% of the ~380 million people worldwide who are suffer from type 2 diabetes [5]. It is harder to treat and typically occurs in adults as a result of excess weight or hormonal imbalances [6]. Type 2 diabetes mellitus has become an epidemic, and virtually no physician is without patients who have the disease [7].

Several pathogenic processes are involved in the development of diabetes. These range from autoimmune destruction of the pancreatic β-cells with consequent insulin deficiency to abnormalities that result in resistance to insulin action [8]. In the long term effects of diabetes mellitus include progressive development of the specific complications of retinopathy with potential blindness, nephropathy that may lead to renal failure, or neuropathy with risk of foot ulcers, amputation, Charcot joints, and features of autonomic dysfunction, including sexual dysfunction. People with diabetes are at increased risk of cardiovascular, peripheral vascular and cerebrovascular disease [9].

Over the years several sources of stem cells have been claimed to cater to the need of insulin producing cells. These include human embryonic stem cells, induced pluripotent stem cells, human perinatal tissues such as amnion, placenta, umbilical cord and postnatal tissues involving adipose tissue, bone marrow, blood monocytes, cord blood, dental pulp, endometrium, liver, labia minora dermis-derived fibroblasts and pancreas [10].

Treatment of Type 2 diabetes is complicated by several factors inherent to the disease process, typically, insulin resistance, hyperinsulinemia, impaired insulin secretion, reduced insulin-mediated glucose uptake and utilization [11]. It is well-known that exercise and diet control are helpful to manage glucose level at initial stage [12]. A novel therapeutic approach to reduce pancreatic β-cells are dysfunctional or altogether absent in diabetic patients, replacement of these cells has become the major target of stem cell research in diabetes [13]. There are a number of different sources of stem cells and the most investigated types of stem cells for DM treatment are: Embryonic stem cells [14], induced pluripotent stem cells of induced pluripotent stem cells [15], germ cell derived stem cells, and mesenchymal stem cells [16].

But, in addition to these therapeutic of DM either in-vivo or in-vitro approaches, the most important problem is choosing the best type of progenitor cell. Tissue Engineering is an interdisciplinary discipline addressed to create functional three-dimensional (3D) tissues combining scaffolds, cells and/or bioactive molecules. Tissue engineering/regenerative medicine strategies require interaction and integration with tissue and cells through incorporation of appropriate physical and cellular signals. Therefore, inclusion of modifying factors such as biologically active proteins and DNA are critical to success [17].

This review will be included to establish a novel tissue engineering approach for diabetes mellitus (DM) by fabricating a tissue sheet composed of pancreatic islet cells for *in vivo* transplantation [18]. One alternative to organ or tissue transplantation is to use a renewable source of cells. Stem cells are clonogenic cells capable of both self-renewal and multiline age differentiation [19]. This review will discuss the current evidence and strategy behind these stem cell sources, as well as the advantages and disadvantages of each [13]. Therefore, treatment strategies for DM should be aimed at restoring beta cell mass and/or function, in addition to improving insulin sensitivity. The aim of this review is to give an overview of the existing knowledge of current experimental strategies in the treatment of DM covered by tissue engineering and regenerative medicines [20].

Current and future cell-based therapies of DM

The methods for generating pancreatic beta-cells include a method of creating pancreatic beta-cells in vitro and implanting them into the body and a method of regenerating pancreatic beta-cells in the body via gene introduction or the administration of differential proliferation factors to the body. Moreover, the number of pancreatic beta-cells is also low in type 2 diabetes, caused by the compounding factors of insulin secretory failure and insulin resistance; therefore, if pancreatic beta-cells can be regenerated in a living body, then a further amelioration of the pathology can be expected. The development of pancreatic beta-cell-targeting regenerative medicine can lead to the next generation of diabetes treatment [21].

Curative therapy for diabetes mellitus mainly implies replacement of functional insulin producing pancreatic β cells, with pancreas or islet-cell transplants. However, shortage of donor organs spurs research into alternative means of generating β cells from islet expansion, encapsulated islet xenografts, human islet cell-lines, and stem cells. Stem-cell therapy here implies the replacement of diseased or lost cells from progeny of pluripotent or multipotent cells. Both embryonic stem cells (derived from the inner cell mass of a blastocyst) and adult stem cells (found in the postnatal organism) have been used to generate surrogate β cells or otherwise restore β-cell functioning [22]. Cell therapies with human embryonic and adult stem cells have emerged as an alternative management for various diseases. These cells were able to proliferate and differentiate into various cell types including those bearing a phenotype of insulin-secreting β-cells [23].

Stem cells

Stem cells possess an exceptional quality to replenish itself and to produce any specialized cell types under appropriate microenvironment. A rapidly dividing stem cell produces two new cells, each having two choices depending upon the requirement of the organism. Thus, a newly produced cell either may remain as a stem cell or it may undergo further differentiation to become a more specialized cell with specific function [24]. The stem cells have the potential to become any type of specialized cell such as a myocyte, blood cell, hepatocyte and brain cell (Figure 1).

Embryonic stem cells

Many cell signaling and epigenetic factors involved in the differentiation process are still unknown, although the presence of markers such as *PDX1*, *Isl1*, and *Foxa2* are indicative of pancreatic β-cells. The exact composite and temporal progression of transcription factors present in pancreatic cells is important for

identification, as many of these factors are seen in different combinations in other cell lineages. The differentiation process is meant to mimic the embryological development of the pancreas [13].

Pancreatic and duodenal homeobox 1 (Pdx1) is a transcription factor that regulates the embryonic development of the pancreas and the differentiation toward β cells. Previously, we have shown that exposure of mouse embryonic stem cells (mESCs) to high concentrations of diethylenetriamine nitric oxide adduct (DETA-NO) triggers differentiation events and promotes the expression of Pdx1. Here we report evidence that Pdx1 expression is associated with release of polycomb repressive complex 2 (PRC2) and P300 from its promoter region [25].

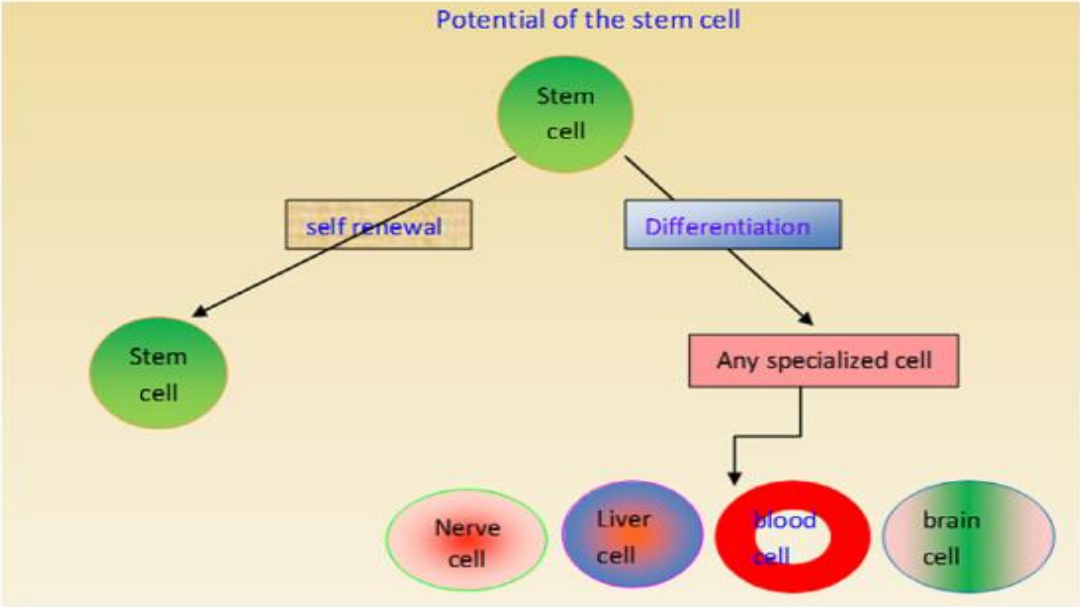

Figure 1. Self-renewal and differentiation potential of the stem cells [26].

TISSUE ENGINEERED PANCREATIC SUBSTITUTES

Tissue restoration is the process whereby multiple damaged cell types are replaced to restore the histoarchitecture and function to the tissue. Several theories, have been proposed to explain the phenomenon of tissue restoration in amphibians and in animals belonging to higher order [27].

A profound knowledge of the development and differentiation of pancreatic tissues, especially islets of Langerhans, is necessary for developing regenerative therapy for severe diabetes mellitus. A recent developmental study showed that PTF-1a is expressed in almost all parts of pancreatic tissues, in addition to PDX- 1 *PDXI*, a well-known transcription factor that is essential for pancreas development [28]. Tissue engineering may use one of three basic strategies: isolated cells or cell substitutes, tissue inducing substances, or cells placed within matrices. For the purposes of IDD, the first approach is already being applied in islet transplantation. Since β-cells do not significantly expand in cell number *in vivo* the second approach of a tissue inducing substitute is considerably more challenging. Alternatively, it has been reported that exocrine pancreas tissue can be induced to take on a β-cell phenotype through metaplasia so a similar approach could be envisioned to target those cells [29].

Mesenchymal stem cells

Curative therapy for diabetes mellitus mainly implies replacement of functional insulin-producing pancreatic β cells, with pancreas or islet-cell transplants. However, shortage of donor organs spurs research into alternative means of generating β cells from islet expansion, encapsulated islet xenografts, human islet cell-lines, and stem cells. Stem-cell therapy here implies the replacement of diseased or lost cells from progeny of pluripotent or multipotent cells. Both embryonic stem cells (derived from the inner cell mass of a blastocyst) and adult stem cells (found in the postnatal organism) have been used to generate surrogate β cells or otherwise restore β-cell functioning [22].

Originally identified by Friedenstein et al. in 1976 [30] as a fibroblast-like cell population capable of generating osteogenic precursors, the mesenchymal stromal cells derived from the bone marrow (BM) are a

rare, heterogeneous, stromal population of multipotent non-haematopoietic progenitor cells with the capacity to differentiate into multiple mesenchymal lineages, including bone, fat and cartilage. Due to this characteristic, Caplan [31] dubbed them "mesenchymal stem cells" (MSCs), which has been recently changed by a consensus statement recommendation to "multipotent mesenchymal stromal cells" [32]. Other studies have identified pluripotent cells capable of differentiation along endodermal and neurectodermal lineages, including neurons, hepatocytes and endothelial cells [33], [34]. Such stem cells, isolated from BM, have been referred to as "multipotent adult progenitor cells" (MAPCs), "marrow-isolated adult multilineage inducible cells" (MIAMIs) [35] and "very small embryonic-like stem cells" (VSELs) . However, even if the transdifferentiation capacities of these primitive cell types is of major interest, obtaining them requires highly specific culture conditions and, so far, it has not been possible to isolate these cells from fresh BM. Whether or not they represent a culture phenomenon remains an unanswered question [36].

MSCs administration can prevent and treat diabetic nephropathy, which is a complication of DM and is defined as progressive kidney disease caused by angiopathy of the capillaries supplying the kidney glomeruli. MSCs have been used for the treatment of diabetic nephropathy in nonobese diabetic/severely compromised immunodeficient (NOD/SCID) and C57 black 6 (C57/BL6) mice, which succumb to DM after application of multiple low doses of STZ. About 30–60 days after STZ injection, kidneys of treated mice showed the presence of abnormal glomeruli characterized by increased deposits of ECM protein in the mesangium, hyalinosis, and increased number of macrophages in the glomeruli [37].

Induced pluripotent stem cells

The use of iPSCs untangles regenerative therapy in diabetes from ethical constraints, but also poses its own unique challenges. The production of iPSCs from human fibroblasts was first demonstrated by Yamanaka and colleagues through retroviral transduction of four transcription factors (*Oct-3/4, Sox-2, Klf-4*, and *c-Myc*) in a process termed direct reprogramming. In lieu of the high tumorigenic potential of direct reprogramming resulting from genome integration and activation of oncogenic *c-Myc*, additional research proved iPSCs could be produced from somatic cells in the absence of *c-Myc*, but at the expense of efficiency [13]. Engraftment of mature insulin producing cells derived from induced pluripotent stem cells may represent the most promising treatment strategy for diabetic patients with impaired β-cell function [13].

β cells from direct reprogramming

One theme that has been explored extensively by researchers is to create new β cells from existing pancreatic cells. The rationale behind this approach is that because these cells are either β-cell precursors or developmentally related to β cells, the barrier to reprogramming them into functional β cells may be lower than in cells that are not as closely related developmentally.

In normal healthy conditions β-cells have a long life-span with a low proliferation rate [38]. In response to increased metabolic demand or after injury, however, the adult pancreas maintains or acquires the ability to produce new cells, particularly β-cells. The precise identification of the mechanisms involved in the maintenance of β-cell mass under different conditions could offer new hints to help generating new β-cells as a cell replacement therapy for treating diabetes [39].

Today, insulin-dependent patients rely on daily insulin injections. Transplantation of isolated islets from cadavers is problematic due to donor scarcity (about 6000 islets/kg of body weight are required [40], and is only applicable to certain forms of diabetes; in addition, transplantation has met with limited success due to restricted engraftment survival [41]. A promising approach relies on devising unlimited *in vitro* generation of insulin-producing cells derived from embryonic stem (ES) cells or, even more interestingly, from patient-derived induced pluripotent stem (iPS) cells [42]. Very recently, however, in view of new experimental evidence showing that adult differentiated pancreatic cells can reprogram and change their phenotype [43], exploration of the intrinsic spontaneous capacity of the adult pancreas to regenerate β-cells, in particular from heterologous origins, has acquired a new dimension as a route to the development of therapeutic treatments for diabetes [44].

This review will focus on β-cell regeneration and its diverse mechanisms. In fact, exploiting the intrinsic capacity of the adult pancreas to produce new β-cells endogenously is probably the most promising way to develop cell replacement therapies to treat the forms of diabetes that result from massive β-cell loss. Nevertheless, a prerequisite for such an achievement will be to uncover the immunological basis of the pathogenesis of the disease. (Reference)

Antigen-presenting cells

So far, at least 15 distinct peptides derived from β-cells and their corresponding CD4+ T cells have been identified [45]. The presentation of β-cell antigens is a complex issue as β-cells themselves do not express MHC class II molecules. It can be surmised that presentation of β-cell-specific antigens is mediated by Antigen-Presening Cells (APCs) within islets of Langerhans. These professional dendritic cells (DCs) are able to load the peptide groove of their MHC class II complexes with peptides derived from β-cell granules [46]. In this context, local lymph nodes draining the pancreas are crucial to the selection and activation of diabetogenic T cells [47]. Here, the question arises, how the β-cell antigen presentation takes place. It is not clear yet, whether this occurs via migration of islet DCs to the lymph nodes or, instead, by drainage of β-cell products directly to the nodes and subsequent uptake by DCs in the draining lymph nodes. Based on our knowledge gathered from the NOD mouse, β-cell autoimmunity progresses in relatively well-defined "checkpoints". A first checkpoint is marked by DC infiltration of islets in 2- to 3-week-old NOD mice. Early detection of DCs and macrophages is followed by CD8+ and CD4+ T cells, NK cells, and B cells. During islet cell infiltration these cells encounter β-cell autoantigens such as GAD65 and islet-specific glucose-6-phosphatase catalytic subunit-related protein (IGRP). The β-cell destruction resulting from inflammatory damage leads to release of cell contents including GAD65 and other autoantigens. Subsequently, these can be taken up by activated endothelial cells able to process and present disease-related epitopes of the GAD65 autoantigen [48].

Current and future cell-based therapies

Recently, Andreas Lechner and colleagues failed to see transdifferentiation into pancreatic β cells after transplantation of bone-marrow cells into mice [49]. Last year, Jayaraj Rajagopal and colleagues failed to derive β cells from embryonic stem cells [50]. However, others have seen such effects [51].

CONCLUSION

To date, no fully defined and clinically applicable stem cell, tissue engeenring and adult β-cell stem/progenitor has been isolated. Nevertheless, studies of the development and the physiology of the pancreas make the existence of pancreatic stem/progenitor cells highly likely. Additionally, several potential candidate cells are being studied, and although more rigid experimental criteria have yet to be met, the published results look highly promising. The utilization of adult stem/progenitor cells for the generation of insulin-producing β-cells in vitro and their use for the treatment of diabetes, therefore, seem to be feasible in the near future.

DECLARATIONS

Authors' contributions

MB conceived the review, coordinated the overall activity, and reviewed the manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgment

The authors' heartfelt thanks University of Gondar, Research and Community Service V/President Office, Collage Veterinary Medicine and Animal Sciences for the finance and resource supporting

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2019 SCIENCELINE
Journal of Life Science and Biomedicine
J Life Sci Biomed, 9 (4): 109-116, 2019

ISSN 2251-9939

Comparative study of two methods of anterior cruciate ligament reconstruction with lavsan (polyethylene terephthalate)

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ABSTRACT

Introduction. The anterior cruciate ligament (ACL) is one of the main stabilizateur of the knee joint. Many methods were suggested for its reconstruction with different allo/autografts, as well as synthetic materials. Aim. The study aimed to compare two methods of ACL reconstruction with lavsan (polyethylene terephthalate). Methods. The study included 102 patients who underwent ACL reconstruction with lavsan tape (polyethylene terephthalate). Group 1 (46 patients) underwent single-bundle ACL reconstruction, and group 2 (56 patients) underwent double-bundle reconstruction. Patients were evaluated with Lachman, anterior drawer and pivot-shift tests and Lysholm score. Results. Our results showed better results in double-bundle group, especially rotational stability was significant better. Besides that majority of patients of I group had some problem flexion of the operated knees. Conclusion. Independent of the method of ACL reconstructions these surgeries must be perform taking into account anatomic features and changes of the knee. Double-bundle technique of ACL reconstruction with lavsan provides better stability than single-bundle technique.

Original Article

PII: S225199391900017-9

Rec. 15 June 2019
Rev. 22 July 2019
Pub. 25 July 2019

Keywords
Anterior Cruciate Ligament, Single-Bundle Technique, Double-Bundle-Technique, Synthetic Material

Abbreviations: ACL: Anterior cruciate ligament, BTB: Bone-tibia-bone, LARS: Ligament advanced reinforcement system, AM: Antero-medial, PL: Postero-lateral

INTRODUCTION

Anterior cruciate ligament is one of the stabilizing structures of the knee. The incidence of ACL ruptures increased in recent times, and today ACL reconstruction is one of most frequently performed surgeries in orthopaedics [1]. ACL ruptures may lead instability of the knee which results in disability of the knee in cutting and pivoting activities [2]. Unstable knee after ACL ruptures result in following meniscus injuries, degenerative changes of articular surfaces of knee [2, 3]. The goal of ACL reconstruction is stabilization of the knee; minimize risk factors of the risk of re-injury, to return previous activity of sportsmen. At present time, single and double-bundle methods of ACL reconstruction are used. Each technique has its indications and contraindications [2]. It is necessary to take into account anatomic and individual characteristics of the patient to choose a method of surgery.

A single-bundle ACL reconstruction means to restore the native anatomy of ACL as closely as possible and to achieve normal knee biomechanics [2]. In order to achieve it is necessary to follow the following principles: 1) to observe and to objectify native anatomy of patients; 2) to individualize each surgery according patient's anatomy; 3) to place the tunnels and grafts at in the centre of patient's footprints; 4) to re-establish knee biomechanics by tensioning of the graft. In this method femoral and tibial tunnels must be positioned midway between the centres of AM and PL insertion sites.

Double-bundle reconstruction of ACL is explained with anatomic structure of ACL. ACL consists of two parts: antero-medial (AM) and postero-lateral (PL) bundles [1]. Both bundles are synergists but in different position of the knee they have different functions. Insufficiency of AM bundle shows increased antero-posterior translation of the tibia like in complete ACL rupture. Insufficiency of PL bundle results in instability with pivoting and turning. In double-bundle ACL reconstruction AM and PL tunnels are drilled separately at the

native femoral and tibial sites. In both methods femoral tunnels can be drilled with using a transtibial or medial portal technique [1, 2]. Double-bundle reconstruction of ACL introduced to achieve better stability, particularly more stability for rotator loads [4, 5]. Some studies demonstrated that inability of single bundle reconstruction to restore intact knee rotational stability [1]. But there are studies that don't show differences between a single-bundle and double-bundle technique, when placed anatomically and customized to the patient's anatomy [6-9].

Despite at present time ACL reconstruction with auto- and allografts is popular, synthetic artificial ligaments are still used [3]. One of them is polyethylene terephthalate (lavsan), there are many reports about ACL reconstruction with this artificial ligament. Lavsan is a non-absorable synthetic material containing polyethylene terephthalate fibres [10]. The use of artificial ligaments based on lack of donor comorbidity, reduced operation time, abundant supply and enough strength and early loading of the operated extremity that result in shortening of rehabilitation period [3, 11-13]. Parchi et al. [14] proposed the use of a synthetic graft for the ACL reconstruction to all patients older than 30 years with a symptomatic isolated ACL injury in order a quick return to their previous sport activity level as a possible alternative to the autograft. Pan et al. [15] reported about the similar results obtained at midterm follow-up in groups between bone –patellar-bone (BTB) and LARS groups. Huang et al. [13] concluded that the LARS® artificial ligament has excellent biomechanical properties in comparing with autologous and allogenic tendons that means LARS artificial ligament can be widely used for ACL reconstruction. Therefore, the aim of study was to compare two methods of ACL reconstruction with lavsan (polyethylene terephthalate).

MATERIAL AND METHODS

Our study was included 102 patients with ACL rupture who underwent ACL reconstruction with synthetic material (lavsan tape). Assessment was made with Lachman, anterior drawer and pivot-shift tests and Lysholm knee scoring scale. First group included 46 patients (42 male, 4 female) who underwent single-bundle (SB) technique. Lachman test was positive in all patients of this group: 3-5 mm (n=32), 6-10 mm (n=14). Anterior drawer test was negative in 4 patients, positive 3-5 mm (n=32), 6-10 mm (n=10). Pivot shift was negative in 18 patients, positive 1+ (n=20), positive 2+ (n=8). A mean Lysholm score on this scale ranged was 57 to 72 points (mean 64 points). Second group included 56 patients (49 male and 7 female), who underwent ACL reconstruction with double-bundle (DB) technique. Lachman test was positive in all patients of this group: 3-5 mm (n=42), 6-10 mm (n=16). Anterior drawer test was negative in 8 patients, positive 3-5 mm (n=41), 6-10 mm (n=7). Pivot shift test was negative in 8 patients, positive 1+ (n=35), positive 2+ (n=13). A mean score on Lysholm scale ranged from 55 to 74 points (mean 62 points).

The aim was to compare results of both techniques of ACL reconstruction that are made under spinal anesthesia in supine position of patient. Surgeries were performed by different doctors of the same department who were masters of arthroscopic surgery. An arthroscope is inserted inside of the knee with using routine anterolateral and anteromedial portals. First all knee structures is inspected carefully, including meniscus, articular cartilage, synovial membrane. In case of meniscus tear the torn part of meniscus is resected. Then ACL reconstruction is performed using single- or double-bundle technique depending on patient's conditions, anatomy and individual parameters.

Single-bundle technique of ACL reconstruction with lavsan tape

After arthroscopically revealing ACL rupture the knee is flexed to 110° and a femoral tunnel is drilled at centre of insertion site of ACL using an anteromedial portal technique. First it is drilled with guide pin, then with drill diameter of 4 mm along the whole lateral condyle of the femur.

After that knee flexed under 90° and the tip of the conductor is put to the insertion site of the centre of ACL. A conductor is placed on 45-50° to the articular surface of plateau of the tibia, approximately 3.5-4 cm medially from the tibial tuberosity. On this area an incision of 1.5 cm length is made. First it is drilled with a guide pin from this incision inside of the knee, and then the tunnel is drilled with a drill of 4 mm diameter. After drilling tunnels, first end of the lavsan tape of 5 mm width is passed first to the tibial and femoral tunnels respectively. The end of the lavsan tape is pulled out outside of lateral condyle of the femur, length of pulled out tape must be minimum 5 cm of length. Then 2 cm incision is made of medial condyle area, just near the insertion site of the medial collateral ligament to the femur. A surgical clamp is inserted from this incision between joint capsule and fascia, and directed distally, that is to the 1.5 mm sized incision on the anteromedial part of proximal tibia. Then the second end of the lavsan tape is fixed with a surgical clamp and pulled out from the incision on medial condyle of the femur.

Drilling of transversal tunnel in the femur

Then it is drilled a transversal tunnel with a guide wire from the medial condyle to the lateral condyle of the femur. After that it is drilled with 4 mm drill of diameter. Second end of the lavsan is passed from the transversal tunnel (from medial the condyle to the lateral condyle) and pulled out on the lateral femoral condyle area. Length of the free end of the lavsan tape must have 5 cm from a skin. The scheme of surgery is prescribed on figure 1.

After pulling out of both ends of lavsan tape, 3 cm sized incision is made above on lateral femoral condyle between both ends of the lavsan tape. Both ends are pulled out from this incision, soft tissues separated till the bone tissues and are tied into a knot (Figure 2). The extra ends of the lavsan tape above the knot are cut. Drainage of wounds is made, sutures is put. Aseptic bandages. MRI is made after surgery (Figures 3 and 4).

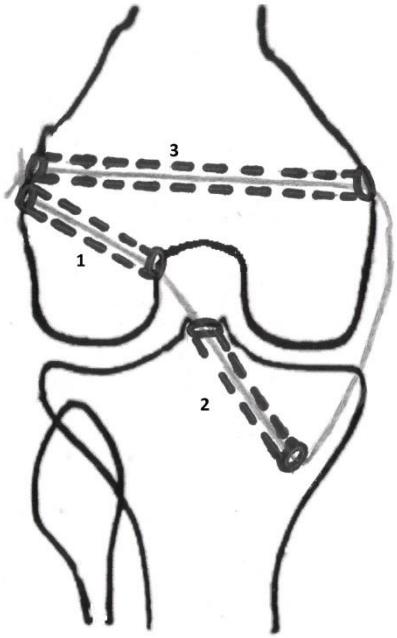

Figure 1. The scheme of single bundle ACL reconstruction with lavsan tape.

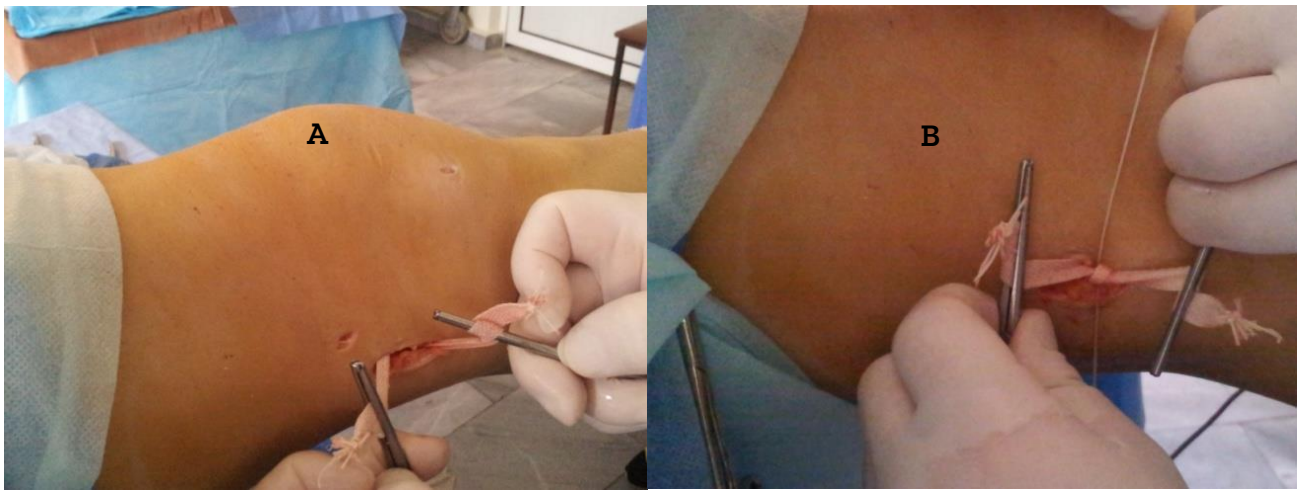

Figure 2. A) Pulling out of both ends of the lavsan tape from the same incision; B) Knotting of both ends of lavsan tapes.

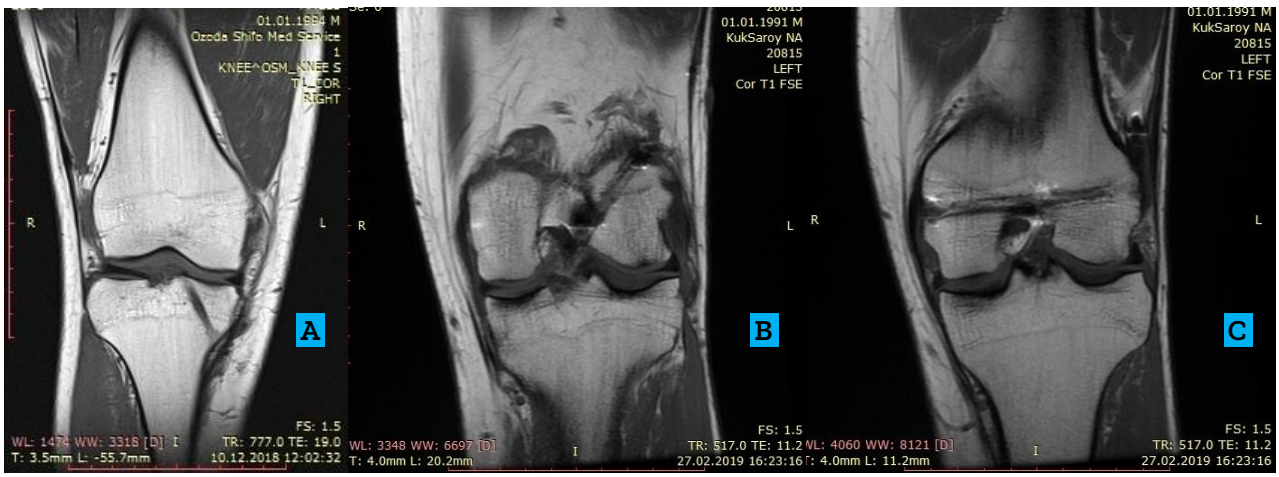

Figure 3. MRI of patient after surgery. A) tibial tunnel on the right tibia;B) femoral tunnel of the left femur;C) transversal tunnel of femur of left femur.

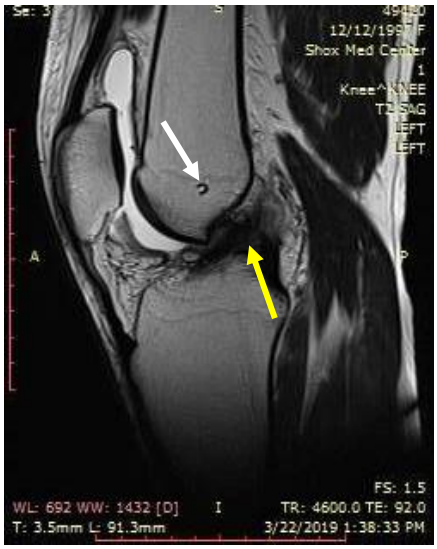

Figure 4. MRI of patient in 18 month after single-bundle ACL reconstruction technique. It is seen a ligamentization of the lavsan tape (yellow arrow) and a hole of the transversal tunnel in the femur (white arrow).

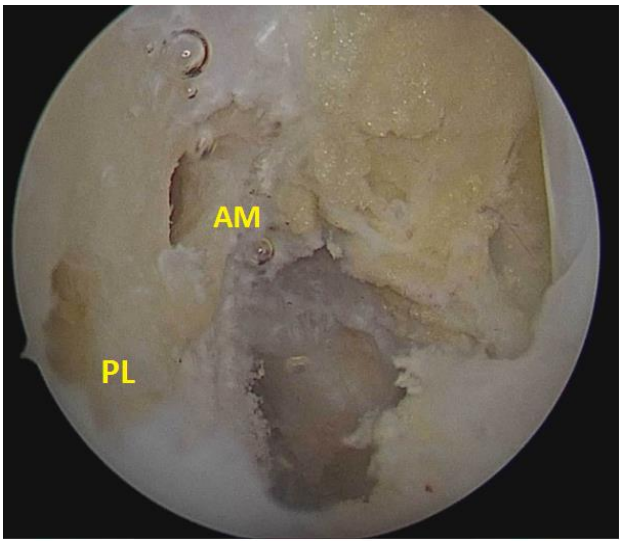

Figure 5. Arthroscopic view of drilled femoral tunnels. AM: anteromedial tunnel, PM: posterolateral tunnel.

Double-bundle technique of ACL reconstruction with lavsan tape

The same arthroscopic portals are used for double-bundle technique. After arthroscopically revealing of ACL rupture the knee is flexed to 110° and two femoral tunnels is drilled at insertion sites of both bundles of ACL. First tunnel is drilled at insertion site of PL (posterolateral) bundle of ACL. It is drilled with guide pin first, then with drill diameter of 4 mm along the whole lateral condyle of the femur. In order to make the second tunnel a drill bit put to the insertion site of AM (anteromedial) bundle and it is drilled with guide pin first, then with drill diameter of 4 mm along the whole lateral condyle of the femur (Figure 5). After that knee flexed under 90° and the tip of the conductor is put to the insertion site of PL bunble of ACL at tibia. Conductor is placed on 45-50° to the articular surface of plateau of the tibia, approximately 3.0-4 cm medially from the tibial tuberosity. It is drilled with guide pin first, then with drill diameter of 4 mm from outside to inside (tunnel 3). Then the tip of the conductor is put to the insertion site of AM bunble of ACL at tibia. The conductor is placed on 60-65° to the articular surface of plateau of the tibia, approximately 1.5-2 cm medially from the tibial tuberosity. It is drilled with guide pin first, then with drill diameter of 4 mm from outside to inside (tunnel 4). After drilling tunnels, one end of the lavsan tape of 5 mm width is inserted first to the tunnel 3 (PL tunnel of tibia), then tunnel 1 1-tunnel (PL tunnel of femur) respectively. End of the lavsan tape is pulled out outside with minimum 5 cm length on lateral condyle of femur. Second end of the lavsan tape is inserted first tunnel 4 and tunnel 2 respectively (AM tunnels of tibia and femur respectively), then this second end is pulled out on the lateral condyle of femur with minimum 5 cm length on lateral condyle of femur. After pulling out of lavsan tapes 3.0 cm sized incision is made above on lateral femoral condyle (the scheme of double-bundle-technique is prescribed on figure 6). Both ends of the lavsan tape are pulled out from this incision and tied into a knot (Figure 2). The extra ends of the lavsan tape above the knot are cut. Drainage of wounds is made, sutures is put. Aseptic bandages. With this way AM and PL bundles of ACL is created with a lavsan tape (Figure 7). MRI is done after surgery (Figure 8).

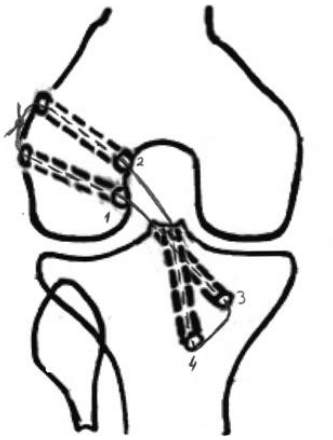

Figure 6. Scheme of double-bundle ACL reconstruction. 1) PL tunnel in the femur, 2) AMtunnel in the femur, 3) PL tunnel in the tibia, 4) AM tunnel in the tibia.

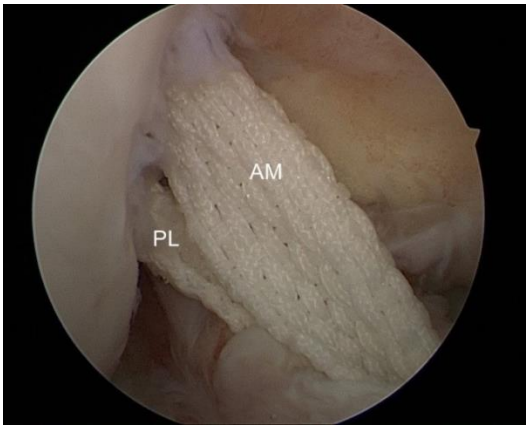

Figure 7. Arthroscopic view after double-bundle ACL reconstruction with lavsan tape. AM: anteromedial bundle, PL: posterolateral bundle.

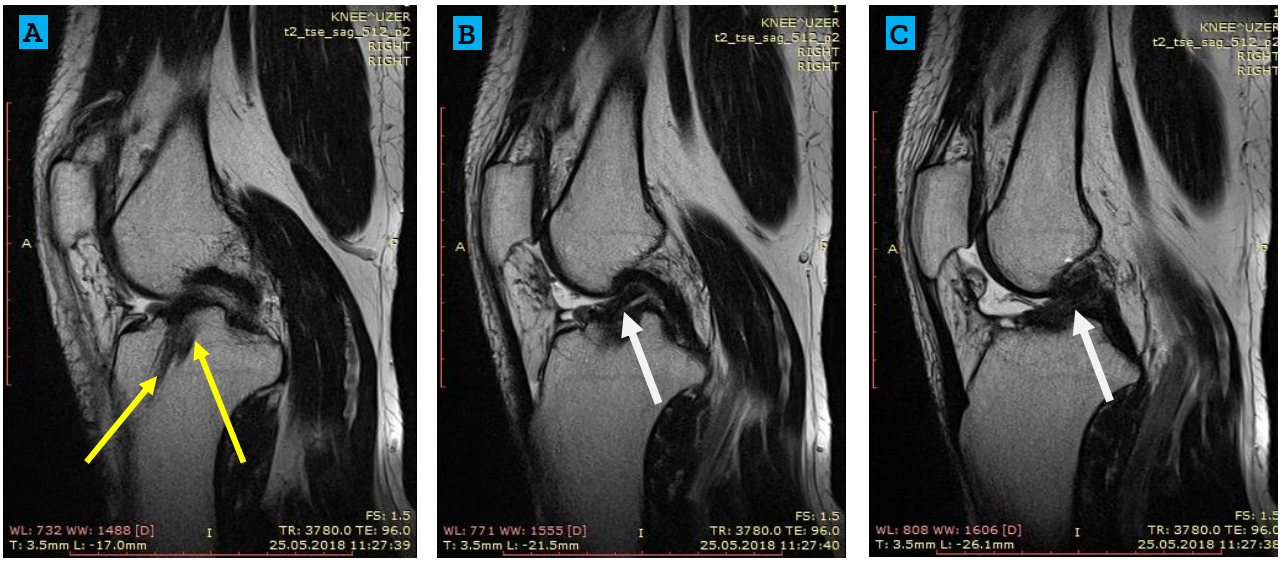

Figure 8. MRI of patient with double-bundle technique in 1 year after surgery. A) drilled femoral tunnels (yellow arrows). B, C). Ligamentization of lavsan tape is seen (white arrow).

Postoperative treatment is done by a standard management of ACL reconstructed patients. Plaster cast was put to the operated extremity for 10-12 days period. In order to prevent hemarthrosis and swelling ice packs were put regularly 10-15 minutes per hour to operated knees up to 10-12 days. From the next day of surgery isometric exercises of the knee were recommended to prevent hypotrophy of muscles. Medications (antibiotics, anticoagulants, anti-inflammation remedies and etc.) are recommended following standards of treatment. Walking was permitted from the next day of surgery with crutches till 4 weeks. In 10-12 days plaster cast is removed and passive range of motions in the knee (flexion, extension) are recommended. Strengthening exercises of quadriceps muscle are recommended step by step. Return to sport is recommended from 6-9 month after surgery, depending on condition of patients.

Ethical approval

The review board and ethics committee of Republican Specialized Scientific and Practical Medical Centre of Traumatology and Orthopaedics Uzbekistan approved the study protocol and informed consents were taken from all the participants.

RESULTS

All patients were followed up at 14-18 month period. At follow up period all patients of both group felt the state of their knees to become better. No major complications occurred as well as venous thrombosis, pulmonary embolism, intra-articular infection in both groups. Lachman, anterior drawer and pivot-shift tests were checked at follow up and patients accessed with Lysholm score. Concerning results of antero-posterior stability results were better in group 2. Lysholm score was higher in group 2 in compared to group 1. Concerning of pivot shift test better results achieved in group 2.

Group 1. Lachman test was negative in 39 patients, slightly positive up to 3 mm in 7 patients. Anterior drawer test was negative in 42 patients and slightly positive up to 3 mm in 4 patients. Pivot-shift test was negative in 39 patients, slightly positive 1+ in 7 patients. A mean Lysholm score was grown up to 82 (ranged between 74 to 92).

Group 2. Lachman test was negative in 50 patients, slightly positive up to 3 mm in 6 patients. Anterior drawer test was negative in 53 patients and slightly positive up to 3 mm in 3 patients. Pivot-shift test was negative in all 56 patients. A mean Lysholm score was grown up to 90 (ranged between 86 to 94).

Patients with of 1-group had difficulty with increasing of motions of the knee. 7 patients of the 1-group had knee flexion deficit approximately 15-20°, while 2 patient of 2-group had knee flexion deficit who has osteoarthritic changes (Figure 9). Synovitis occurred in 6 patients (3 patients from group 1, 3 patients from group 2) till 2-3 months period after surgery. Synovitis was successfully treated with anti-inflammation remedies, ice packs, antibiotics, and intra-articular glucocorticosteroids.

Table 1. Results of treatment of ACL reconstruction of both groups

Groups		Lachman test			Anterior drawer test			Pivot shift test		
		Negative	3-5 mm	6-10 mm	Negative	3-5 mm	6-10 mm	Negative	+	++
Group 1	Preop: Before surgery	-	32	14	4	32	10	18	20	8
	Postop: After surgery	39	7	-	42	4	-	39	7	-
Group 2	Preop: Before surgery	-	39	17	8	41	7	8	35	13
	Postop: After surgery	50	6	-	53	3	-	56	-	-

Figure 9. Range of motions after surgery. A) Patient in 18 motnth after singe- boundle ACL reconstruction with lavsan. There is knee flexion deficit for 20 dg. B) Patient in 12 month after double- boundle lavsanoplasty. No restriction of range of motions.

DISCUSSION

Many studies showed that results of ACL reconstruction with artificial ligaments were successful [3, 15-17]. Krudwig [12] reported about good results in patients with their satisfaction and anteroposterior stability in patients with artificial Trevira-Hofest devices. Lavoi et al. [18] reported about good clinical results with using LARS artificial ligament at 8-45 follow up in 47 patients. But there are many reports about complications of artificial ligament (tear, foreign-body reactions, synovitis, recurrent instability) [11, 19, 20-22]. Gao et al. [23] reported about developed only one case of synovitis (from 159 patients) with overall complications rate 5,7% after ACL reconstruction with LARS in his a multicenter study in with 3- to 5-year follow up.

In our study we watched synovitis in a few patients, who were prescribed medications and ice packages, in severe synovitis we used puncture of the operated knee with administering glucocorticosteroids. Our patients of 1-group felt pain and difficulties during active flexion of operated knee, especially flexion after 90 dg. It is explained with a non-anatomical position of the second end of lavsan tape. Perhaps, direction of the second end of a lavsan tape carried from the medial part of proximal tibia and its transversal direction from the medial condyle to the lateral condyle bothered to achieve full range of motion of the knee.

Struewer et al. [17] and Lee et al. [24] reported about synovial coverage of grafts during second look arthroscopy after ACL reconstruction with augmentation with an artificial ligament. Despite we did not perform second look arthroscopy we watched a ligamentization of artificial grafts in MRI made after at least a year after surgery in both methods.

It is necessary to take into account details, which depends also on human factor. There are two problems which affects the functional outcome of primary ACL reconstruction. First is a correct femoral and tibial tunnel placement. If drill the tunnel too anteriorly on the femoral condyle it may lead to reduced knee flexion and instability of the knee. If drill the tunnel too posteriorly on the lateral femoral condyle it may lead to reduced extension.

Second is a persisting instability after single-bundle ACL reconstruction [1]. ACL reconstruction focused only AM bundle reconstruction ignoring PL bundle leads to rotational instability. It is necessary to take attention that pivot-shift test is not objective but subjective assessment, it is done manually. The speed of the procedure, a magnitude of force applied to the knee and the abduction angle of the hip depends on examiner [25]. Several studies showed that there are not significant differences of results between single-and double-bundle technique when the graft placed anatomically [7, 8].

CONCLUSION

Our study showed that double-bundle reconstruction of ACL with lavsan provided better results than single-bundle technique. It was seen especially in rotational stability. Besides that there were not problems of double-bundle group with restricting of range of motions of operated knee. In choose ACL reconstruction technique it is necessary to take into account anatomic features and changes of the knee. Thus, on method of ACL reconstruction: single-bundle or double-bundle technique, surgery should be performed according an anatomic double-bundle structure of ACL.

DECLARATIONS

Acknowledgements

This work was supported by, Republican Specialized Scientific and Practical Medical Centre of Traumatology and Orthopaedics Uzbekistan, Tashkent, Uzbekistan

Authors' Contributions

All authors contributed equally to this work.

Competing interests

The authors declare that they have no competing interests.

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2019 SCIENCELINE
Journal of Life Science and Biomedicine
J Life Sci Biomed, 9 (4): 117-121, 2019

ISSN 2251-9939

Hematological and selected biochemical indices in preeclamptic pregnant women attending Elnihoud teaching hospital

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ABSTRACT

Background. Preeclampsia (PE) is a form of hypertensive disorder of pregnancy, leading to maternal and perinatal morbidity and mortality worldwide. It is major obstetric problem in developing countries and affecting 2–10% of all pregnancies. Aim. This study aimed to evaluate hematological and some biochemical parameters in preeclamptic pregnant women attending Elnihoud Teaching Hospital, Sudan, and to compare the findings with the severity of the disease. Methods. A descriptive cross sectional study was carried out in Elnihoud Teaching Hospital with total of forty tow pregnant women as participants (14–45 years old). They were selected from the Wards of the Hospital at admission before starting treatment. Hematological and selected biochemical parameters were measured and analyzed for every preeclamptic patient. Results. The study revealed no significant elevation in plasma total protein, total white blood cells (TWBCs), lymphocytes and mean corpuscular volume (MCV) among severe preeclamptic patients versus mild cases. Decrease with no significant value in hemoglobin level, platelets count (PLT), red blood cells (RBCs) and mean corpuscular hemoglobin (MCH) was observed in severe preeclamptic cases compared to mild preeclamptic cases. Conclusion. It is concluded that measurement of hematological and some biochemical parameters might reflect to some extent the effect of preeclampsia on pregnant women. Recommendation. Further studies with more parameters can provide guidance for the evaluation intervention and management of pregnant women who suffering from PE.

Research Article

PII: S225199391900018-9

Rec. 06 June 2019
Rev. 15 July 2019
Pub. 25 July 2019

Keywords
Preeclampsia, Hypertension, Proteinuria, Papillodema.

INTRODUCTION

Preeclampsia is one of the most serious health problems affecting pregnant women and contributes to both maternal and infant morbidity and mortality worldwide [1]. The disorder is defined by the onset of hypertension (blood pressure 140/90 mm Hg) and proteinuria (0.3 g of protein in the urine within a 24-hour period) during the second half of pregnancy (20 weeks) in a woman with previously normal blood pressure [2]. Although multiple mechanisms and factors have long been recognized, including increased oxidative stress; abnormal placentation; cardiovascular maladaptation to pregnancy; malfunction in genetic, immunological, nutritional, hormonal, angiogenic mechanisms; and inflammation the understanding of the exact pathophysiology of preeclampsia has been elusive [3, 4].

Systemic inflammation can be measured by using a variety of biochemical and hematological markers might provide prognostic and diagnostic clues to diseases related to chronic low-grade inflammation [5-7]. In Sudan there is high prevalence of maternal mortality with PE, and accounting 4.2% of all obstetric complications and 18.1% of maternal deaths [8].

The aim of the current study was to evaluate plasma total protein, hemoglobin, total white blood cells (TWBCs), red blood cells (RBCs), platelets count (PLT), lymphocytes, packed cell volume (PCV), mean corpuscular volume (MCV) and mean corpuscular hemoglobin, or "mean cell hemoglobin" (MCH) as complete blood count for preeclamptic patients attending Elnihoud Teaching Hospital and to compare the findings with the severity of the disease.

MATERIAL AND METHODS

This study was descriptive cross sectional study; carried out in Elnihoud Teaching Hospital, Elnihoud Locality, West Kordufan State, Sudan from January 2018 to December 2018. A total of forty tow pregnant women were included in this study. They were selected from the Wards of the Hospital at admission before starting treatment.

Inclusion criteria

Preeclamptic women with ages 14 – 45 years old, blood pressure ≥ 140/90, and also with proteinuria ≥300mg/24hrs urine collection were included. Preeclamptic patients with blood pressure ≥ 160/110 or/and proteinuria ≥ 1g/ 24 hours urine collection or/and presence of papillodema were taken as severe preeclamptic cases, while preeclamptic patients with blood pressure 159/109 – 140/90, proteinuria 0.3 to 1g/ 24 hours urine collection and absence of papillodema taken as mild preeclampsia.

Exclusion criteria

Pregnant women with pre-gestational diabetes mellitus, primary or secondary lipid disorders, severe anemia, those suffer from any other hematological or endocrine disorders were excluded. Questionnaires were filled and blood samples were obtained for measurement of laboratory parameters by using chemical and hematological analyzers. Data were analyzed by SPSS program version 20.

Ethical approval

The review board and ethics committee of University of West Kordufan for Medical Education and Research approved the study protocol and informed consents were taken from all the participants.

RESULTS

Figure 1 show the ages of participants which were 14 – 20 (28.5%), 21 – 25 (21.5%), 26 – 30 (30.9%) and > 30 (19.1%). Figure 2 shows the parity of the study group, primiparous (45.2%), multiparous (34.7%) and grand multiparous (19.2%). From the entire participants, (76%) have severe preeclampsia and (24%) have mild preeclampsia.

Characteristics and description of the study group

Table 1 shows the characteristics and description of the study group. The occupations of the participants were teacher (2.4%), employee (2.4%), farmer (7.1%) and housewife (88.1%). The study group ages at time of marriage per year were 14-20 (73.8%), 21-25 (14.3%), 26-30 (7.1%) and > 30 (4.8%) years old. Regarding gestational ages at onset of preeclampsia per week they were 20 - 24(9.5%), 24+1 –28(7.1%), 28+1 – 32(19%), 32+1 – 36(40.5%) and > 36(23.9%). The participants having blood pressure ≥ 160/110 represent (42.9%) and those having blood pressure 159/109 – 140/90 were (57.1%)

Laboratory findings of study group

Table 2 shows the laboratory findings of the participants. Proteinuria (dipstick) for the study group were + (19%), ++ (42.9%) and +++ (38.1%), and there was significant elevation in the cases of severe preeclampsia with ++ and +++ (P=0.052). (52.4%) of the participants have proteinuria from 0.3 – 1 and (47.6%) have proteinuria > 1 with significant elevation in sever preeclampsia compared to mild preeclampsia (P=0.002). Plasma total protein for the study group was (33.3%) normal (66.7%) high and no participant having low plasma total protein and there was no significant difference between sever and mild cases. Hemoglobin level for participants was (81%) low, (19%) normal and no patient have high hemoglobin level and there was no significant difference between sever and mild cases. For TWBCs, (83.3%) of participants their TWBCs were normal, (16.7%) have leucocytosis and no one have low TWBCs count, with no significant difference between sever and mild patients. Regarding the RBCs for study group, (11.9%) have low count, (85.7%) their RBCs were in normal range, while (2.4%) have high RBCs count and there was no significant difference between sever an mild cases. Concerning PLT, (38.1%) low PLT, (57.1%) normal PLT count and (4.8%) high PLT count with no significant difference between sever and mild cases. For lymphocytes, (31%) of the participants have normal lymphocytes (69%) have high lymphocytes and no one have low lymphocytes count with no significant difference between sever and mild preeclamptic patients. (2.4%) of entire participants have low MCV, no normal MCV, while (97.6%) have high MCV and there was no significant difference between sever and mild cases. For MCH, (92.9%) of the participants have low MCH, (2.4%) have normal MCH and (4.8%) have high MCH, with no significant difference between sever an mild cases in all.

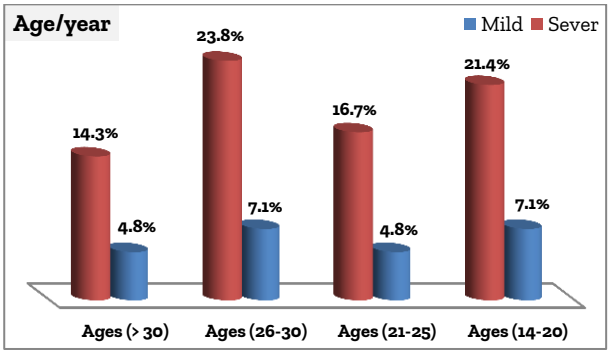

Figure 1. Ages of the study group

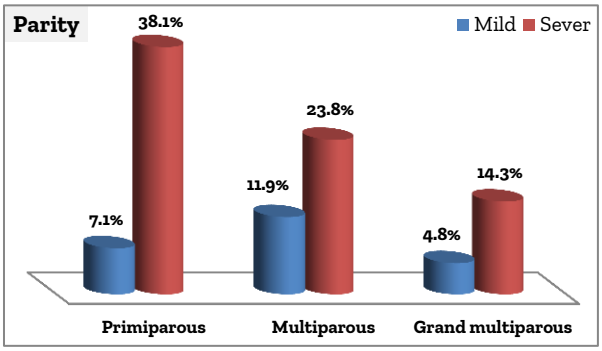

Figure 2. Parity of the study group

Table 1. Characteristics and description of the study group

Character		Preeclampsia status			p-value
		Mild	Sever	Total	
Occupation	Teacher	0	1(3.1%)	1(2.4%)	0.621
	Employee	0	1(3.1%)	1(2.4%)	
	Farmer	0	3(9.4%)	3(7.1%)	
	Housewife	10(100%)	27(84.4%)	37 (88.1%)	
Total		10(100%)	32(100%)	42 (100%)	
Age at time of marriage/year	14 – 20	7(70%)	24(75%)	31(73.8%)	0.693
	21 – 25	2(20%)	4(12.5%)	6(14.3%)	
	26 – 30	0	3(9.4%)	3(7.1%)	
	> 30	1(10%)	1(3.1%)	2(4.8%)	
Total		10(100%)	32(100%)	42 (100%)	
Gestational age at onset of preeclampsia / week	20 – 24	2(20%)	2(6.3%)	4(9.5%)	0.372
	24+1 – 28	0	3(9.3%)	3(7.1%)	
	28+1 – 32	2(20%)	6(18.8%)	8(19%)	
	32+1 – 36	5(50%)	11(34.4%)	17(40.5%)	
	> 36	1(10%)	10(31.2%)	10(23.9%)	
Total		10(100%)	32(100%)	42 (100%)	
Blood pressure	≥ 160/110	0	18(56.3%)	18(42.9%)	0.002
	159/109 – 140/90	10(100%)	14(43.7%)	24(57.1%)	
Total		10(100%)	32(100%)	42 (100%)	

Table 2. Laboratory findings of study group

Character	Preeclampsia status			p-value
	Mild	Sever	Total	
Proteinuria (dipstick)				
+	4(40%)	4(12.5%)	8(19%)	0.052
++	5(50.8%)	13(40.6%)	18(42.9%)	
+++	1(10%)	15(46.9%)	16(38.1%)	
Total	10(100%)	32(100%)	42 (100%)	
Proteinuria				
0.3 – 1	10(100%)	14(43.7%)	24(57.1%)	0.002
> 1	0	18(56.3%)	18(42.9%)	
Total	10(100%)	32(100%)	42 (100%)	
Plasma total protein				
Low	0	0	0	0.451
Normal	2(20%)	12(37.5%)	14(33.3%)	
High	8(80%)	20(62.5%)	28(66.7%)	
Total	10(100%)	32(100%)	42 (100%)	
Hemoglobin				
Low	8(80%)	26(81.3%)	34(81%)	1.00
Normal	2(20%)	6(18.7%)	8(19%)	
High	0	0	0	
Total	10(100%)	32(100%)	42 (100%)	
Total white blood cells				
Low	0	0	0	0.168
Normal	10(100%)	25(78.1%)	35(83.3%)	
High	0	7(21.9%)	7(16.7%)	
Total	10(100%)	32(100%)	42 (100%)	
Red blood cells				
Low	0	5(15.6%)	5(11.9%)	0.335
Normal	10(100%)	26(81.3%)	36(85.7%)	
High	0	1(3.1%)	1(2.4%)	
Total	10(100%)	32(100%)	42 (100%)	
Platelets count				
Low	3(30%)	13(40.6%)	16(38.1%)	0.541
Normal	7(70%)	17(53.1%)	24(57.1%)	
High	0	2(6.3%)	2(4.8%)	
Total	10(100%)	32(100%)	42 (100%)	
Lymphocytes				
Low	0	0	0	1.000
Normal	3(30%)	10(31.2%)	13(31%)	
High	7(70%)	22(68.8%)	29(69%)	
Total	10(100%)	32(100%)	42 (100%)	
Mean corpuscular volume				
Low	1(10%)	0	1(2.4%)	0.238
Normal	0	0	0	
High	9(90%)	32(100%)	41(97.6%)	
Total	10(100%)	32(100%)	42 (100%)	
Mean corpuscular hemoglobin				
Low	9(90%)	30(93.8%)	39(92.9%)	0.192
Normal	1(10%)	0	1(2.3%)	
High	0	2(6.2%)	2(4.8%)	
Total	10(100%)	32(100%)	42 (100%)	

DISCUSSION

Although PE only affects approximately 2%–8% of pregnancies worldwide it is associated with severe complications such as eclampsia, hemorrhagic stroke, hemolysis, elevated liver enzymes and low platelets (HELLP syndrome), renal failure and pulmonary edema in addition to other variable mode of clinical presentation and hematological and biochemical changes . Importantly, there is no "cure" for the disease except for early delivery of the baby and placenta [9].

Hypertension, proteinuria, excessive weight gain and edema are classic clinical manifestations of the preeclampsia [10]. Other features include thrombocytopenia, hyperuricemia, abnormal liver function tests and hemoconcentration [11].

The current study revealed that most of the participants were, marriage at age 14 – 20 years old (73.8%), with sever preeclampsia (76%) their blood pressure 159/109 – 140/90 (57.1%). The present study shows significant increase in proteinuria (dipstick) and proteinuria among the sever preeclamptic participants compared to mild group. The elevation of proteinuria showed by the current study might be attributed to impairment of glomerular filtration and loss of intermediate weight proteins such as albumin and transferrin as consequence of preeclampsia.

The study revealed an elevation in the plasma total protein, TWBCs, lymphocytes and MCV among severe preeclamptic patients versus mild cases but with no significant values. These findings were in agreement with Vilchez et al. [12] and Elgari et al. [13] whom stated similar results. The results of the present study disagree with similar studies results carried out by Hale et al. [14] and Ali et al. [15] whom reported that there was decrease with no significant value in the levels of those parameters in preeclamptic women. The elevation of those parameters which revealed by the present study might be due to endothelial damage that associated with preeclampsia.

For hemoglobin level, PLT, RBCS and MCH the study shows decrease with no significant values in severe preeclamptic cases compared to mild preeclamptic cases. These findings were in accordance with similar studies results carried out by Hale et al. [14] and Ali et al. [15] whom reported that there was no significant decrease in the levels of those parameters in preeclamptic women. In contrast, the PLT result of the current study disagrees into some extent with Imteyaz et al., Yaprak et al. and Han et al. [16-18] whom stated that there was significant decrease in PLT level among severe preeclamptic women. Preeclampsia is associated with hematological system impairment and that is might be the cause of the decrease of those parameters which shown by this study.

CONCLUSION AND RECOMMENDATIONS

Preeclampsia as multisystemic disorder can exhibit its harmful effect on all body organs and systems. Because measurement of some biochemical and hematological parameters is fast and easily applicable, they may be used to evaluate to some extent the effect of preeclampsia on pregnant women. Further studies with more parameters can provide guidance for the evaluation intervention and management of pregnant women who suffering from PE.

DECLARATIONS

Acknowledgements

Many thanks are given to our colleagues in the Faculty of Medicine and Health Sciences and for the staff workers in Elnihoud Teaching Hospital.

Authors' contributions

All authors contributed equally to this work.

Competing interests

The authors declare that they have no competing interests.

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Acceptable Examples (at References section)

For Journals:
1. Hasan V, Sri Widodo M and Semedi B. 2015. Oocyte diameter distribution and fecundity of Javaen Barb (*Systomus Orphoides*) at the start of rainy season in Lenteng River, East Java, Indonesia insurance. J. Life Sci Biomed, 5(2): 39-42. DOI, Link
2. Karen KS, Otto CM. 2007. Pregnancy in women with valvular heart disease. Heart. 2007 May; 93(5): 552–558. DOI, Link
3. Doll MA, Salazar-González RA, Bodduluri S, Hein DW. Arylamine N-acetyltransferase 2 genotype-dependent N-acetylation of isoniazid in cryopreserved human hepatocytes. Acta Pharm Sin B, 2017; 7(4):517-522. DOI, Link

For In press manuscripts (maximum 2):
Hasan V, Sri Widodo M and Semedi B. 2015. Oocyte Diamater Distribution and Fecundity of Javaen Barb (Systomus Orphoides) at the Start of Rainy Season in Lenteng River, East Java, Indonesia insurance. In press.

For symposia reports and abstracts:
Cruz EM, Almatar S, Aludul EK and Al-Yaqout A. 2000. Preliminary Studies on the Performance and Feeding Behaviour of Silver Pomfret (Pampus argentens euphrasen) Fingerlings fed with Commercial Feed and Reared in Fibreglass Tanks. Asian Fisheries Society Manila, Philippine 13: 191-199. DOI, Link

For Conference:
Skinner J, Fleener B and Rinchiuso M. 2003. Examining the Relationship between Supervisors and Subordinate Feeling of Empowerment with LMX as A Possible Moderator. 24th Annual Conference for Industrial Organizational Behavior. DOI, Link

For Book:
Russell, Findlay E, 1983. Snake Venom Poisoning, 163, Great Neck, NY: Scholium International. ISBN 0-87936-015-1. DOI, Link

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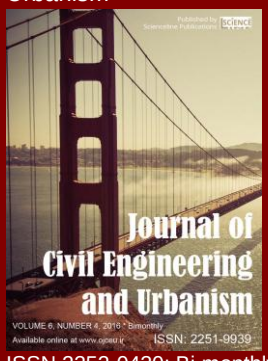

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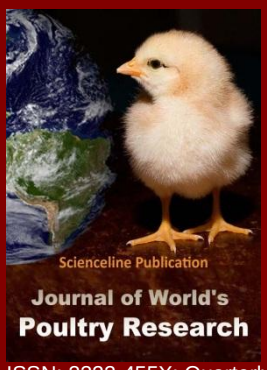

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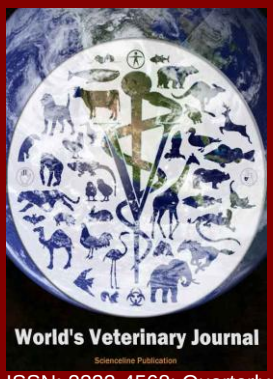

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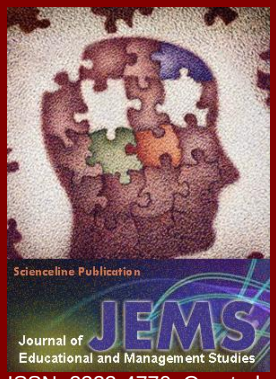

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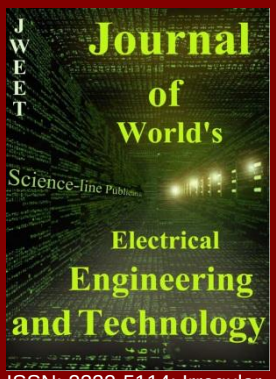

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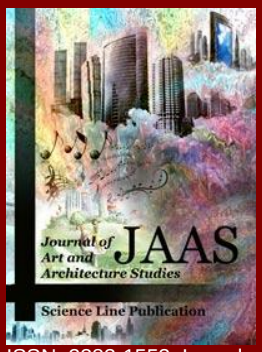

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