

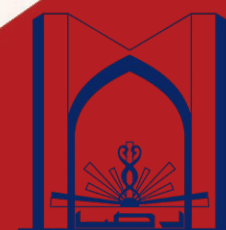
Imam Reza General Hospital Newsletter

Tabriz University of Medical Sciences

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Tabriz University of
Medical Sciences,
Tabriz, Iran



Imam Reza General Hospital,
Tabriz University of Medical
Sciences, Tabriz, Iran

In this issue we read:

An Overview of the Events of the Center and the
Articles of the Respected Professors
and Students

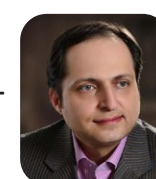
International Educational Programs of Imam Reza General Hospital, Tabriz, Iran¹



• **Mojtaba Mohammadzadeh**
Director-In-Charge's Message
Assistant Professor of Anesthesiology and Intensive
Care Medicine
The head of Imam Reza General Hospital, Tabriz, Iran

Imam Reza General Hospital in Tabriz takes pride in aligning its educational, research, and therapeutic goals with significant progress, achieved with the assistance of esteemed university faculty and officials. To contribute on an international scale, the hospital is organizing both short and long-term educational courses with the help of university professors and responsible authorities, making remarkable strides in this field. In this regard, the honorable deputy for education and research of the center have collaborated to prepare a brochure introducing the mentioned programs in English. It is worth mentioning that the clinical education groups of Imam Reza General Hospital in Tabriz have developed 100 educational programs for applicants from the neighboring countries. I extend my gratitude to all esteemed professors who have participated in this significant project, and invite them once again to demonstrate even greater enthusiasm in presenting their programs. It is hoped that Imam Reza General Hospital in Tabriz and the Tabriz University of Medical Sciences will be recognized as an international hub for education, research, and treatment in the near future in the region.

1. <https://imamreza.tbzmed.ac.ir/?PageID=907>



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The Board of Delegates Cerrahpaşa-Istanbul University Visited Imam Reza General Hospital in Tabriz, Iran



The executive board of Cerrahpaşa-Istanbul University, consisting of the Rector of university, vice Rector of university, and Dean of university along with the university's communications director, visited Imam Reza General Hospital in Tabriz, Iran from December 20th to December 22nd. Over the two days visit and on the first day, a joint session was held with the elite students of Imam Reza General Hospital. The students briefly presented their educational and research backgrounds and shared their perspectives on the fourth-generation university, and the session was well-received by the board of delegates Cerrahpaşa-Istanbul University and the Rector of Istanbul Cerrahpaşa University.

On the second day, group sessions with the educational departments of the hospital were held, which were attended by the directors of each group and their representatives along with the delegation board of Cerrahpaşa-Istanbul University. In this session, the educational groups presented their educational and research activities, expressing their expectations for the collaboration with Cerrahpaşa-Istanbul University. Additionally, short-term and long-term training courses of the hospital were offered to them. Finally, the delegates of Cerrahpaşa-Istanbul University visited three research centers including Immunology, Drug Applied, and Tuberculosis and Lung Diseases centers. These centers received notable attention from the executive board of the delegates of Cerrahpaşa-Istanbul University. Consequently, a comprehensive educational, research, and medical memorandum was signed at all levels, both undergraduate and postgraduate, between the two institutions. Furthermore, Cerrahpaşa-Istanbul University joined the Eurasia University team.



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Artificial intelligence in diagnosis and treatment of Traumatic brain Injury patients

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Artificial intelligence (AI) is increasingly utilized in the diagnosis and management of traumatic brain injury (TBI) patients. Several instances of AI application in TBI diagnosis encompass:

1. Identification and Quantification of Brain Injuries:

AI-based tools are developed to automatically recognize and measure various types of blood in or around the brain, potentially influencing diverse patient outcomes. This technology aims to streamline the detailed assessment of CT scans, particularly in patients with more severe injuries.

2. Contribution to Clinical Care:

AI algorithms exhibit promising outcomes in analyzing CT scans for TBI patients, assisting in the automated identification of traumatic brain lesions, determination of lesion nature and volume, and estimation of patient outcomes. These algorithms are anticipated to be integrated into clinical practice for screening, triage, or indicative prediction to aid human readers.

3. Prognosis Prediction:

Machine learning algorithms are employed to forecast TBI severity and patient outcomes using demographic features, clinical physical examinations, and laboratory data. These algorithms display potential in delivering valuable prognostic insights for TBI patients.

4. Hematoma Detection and Quantification:

AI-driven decision support systems are devised for detecting and quantifying hematomas in TBI patients, enhancing clinical care and management for these individuals.

5. MRI Processing for Invisible Brain Damage:

AI computer programs are harnessed to process MRI findings and detect subtle brain injuries that may elude traditional medical imaging like CT scans. This technology holds promise in designing novel diagnostic tools to comprehend the impact of subtle brain injuries, especially in young athletes.

These instances showcase the varied applications of AI in TBI diagnosis, encompassing the identification of specific brain injuries, prognostication of patient outcomes, and development of decision support systems.

Some illustrations of AI in the management of traumatic brain injury (TBI) patients encompass:

1. Cognitive Rehabilitation: AI-driven cognitive rehabilitation tools are employed to enhance a patient's cognitive functions, physical capabilities, and emotional well-being. These tools offer individualized assistance and aid in formulating tailored treatment strategies for TBI patients.

2. Assistive Technologies: AI-driven assistive technologies, such as smart home devices, are utilized to assist TBI patients in activities of daily living (ADLs) like grooming, dressing, and meal preparation. These technologies can prompt patients to take medications, adapt the environment according to their preferences, and offer accessibility for patients with physical or cognitive limitations.

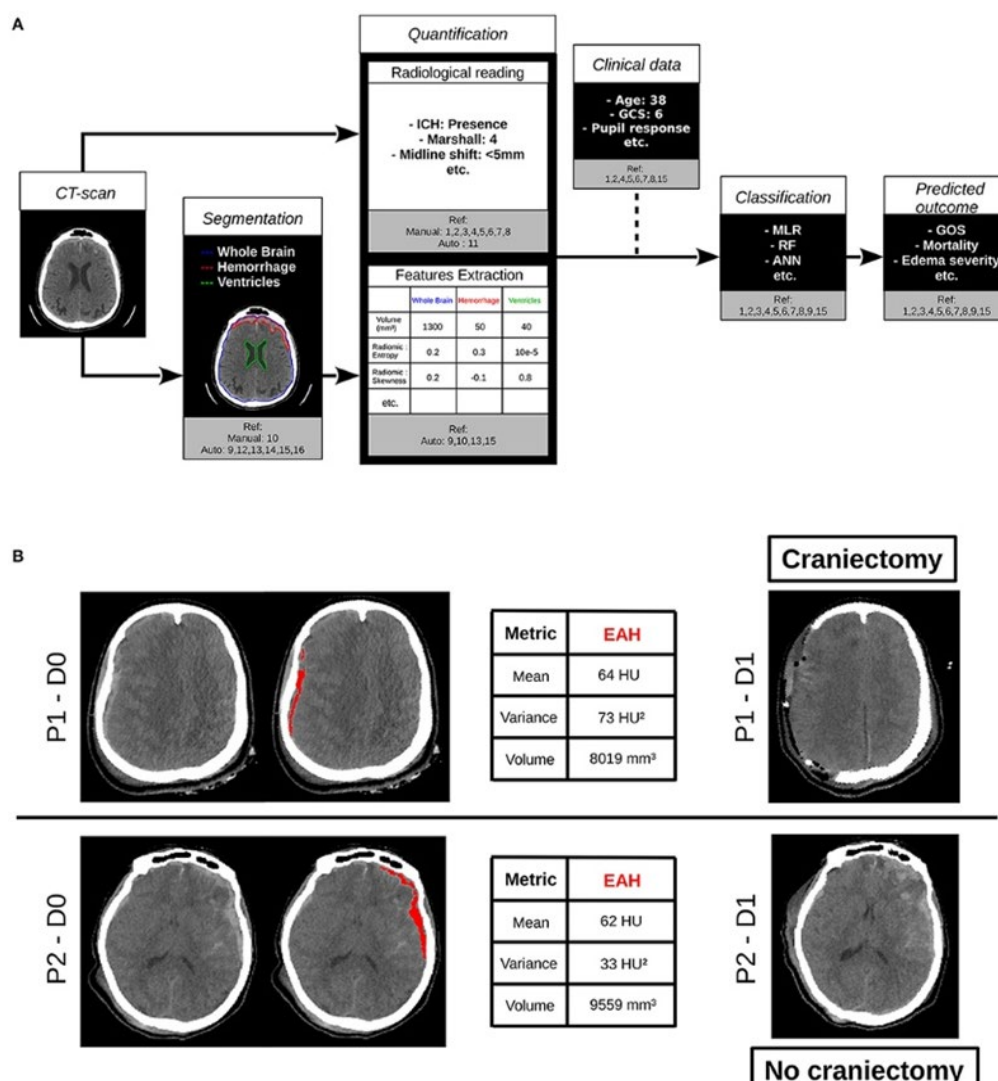
3. Clinical Decision Support: Machine learning models are devised to guide TBI patients towards life-saving interventions by enhancing clinical decision-making early in the treatment continuum. These models can assess patients shortly after admission and enhance clinicians' capacity to make well-informed choices regarding TBI patient management.

These instances underscore the varied applications of AI in the treatment of TBI patients, spanning from cognitive rehabilitation to assistive technologies and clinical decision support.

The utilization of artificial intelligence (AI) in the analysis of computed tomography (CT) scans contributes significantly to the clinical management of traumatic brain injury (TBI) patients. The references and terms are elucidated in Table 1.

An exemplification of AI algorithms in clinical practice is illustrated by the quantification of CT scans for two patients (P1 and P2) at D0 using advanced algorithms. Subsequently, CT scans of the same patients acquired at D1 are presented. Notably, P1 underwent a decompressive craniotomy whereas P2 did not. The largest extra-axial hemorrhage (EAH) lesion was delineated using the Brain Lesion Analysis and Segmentation Tool for Computed Tomography (BLAST-CT), and radiomic metrics were extracted from this region of interest (ROI) as detailed in prior literature. Upon initial inspection, the two lesions exhibit similar profiles in terms of volumes and means; however, the variance of P1 surpasses twice that of P2. This variance could potentially serve as a biomarker warranting further investigation to predict the necessity for craniectomy.

Key terms: ICH (intracranial hemorrhage), GCS (Glasgow Coma Score), MLR (multivariate logical regression), RF (random forest), ANN (artificial neural network), GOS (Glasgow Outcome Score), CT scan (computed tomography image), Ref (References), HU (Hounsfield Units), ROI (region of interest), EAH (extra-axial hemorrhage), D (day).



Adopted from: <https://www.frontiersin.org/research-topics/15936/traumatic-brain-injury--novel-strategies-targeting-the-secondary-injury/articles>

Venous Thromboembolism in Pregnancy and Postpartum

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Pregnancy and puerperium (i.e., postpartum period) are well-established risk factors for Venous thromboembolism (VTE) with a prevalence of 1 in 1600 pregnancies. PE is presently the sixth leading cause of the maternal mortality (%9) in the United States. Several studies have reported an equal distribution of VTE during the trimesters of pregnancy. VTE in pregnant women pregnancy is 4 to 50 times higher compared to than that in non-pregnant women. Increased risk for VTE is reaches its highest level in the postpartum period. VTE is two to five times more common postpartum than the antepartum period.

The risk is the highest in the first six weeks postpartum, but it declines to the rates that are approximately equal to the rates observed in the general population by about 13 to 18 weeks.

The ideal approach to diagnosing PE in pregnancy requires a high index of clinical suspicion while avoiding over-testing. Such an approach ensures that few cases of PE are missed and minimizes the risk of radiation and contrast exposure.

• ANTEPARTUM RISK FACTORS:

These factors include multiple births, varicose veins, inflammatory bowel disease, urinary tract infection, diabetes, hospitalization for non-delivery reasons (particularly those >3 days), BMI ≥ 30 kg/m², and increased maternal age ≥ 35 years.

• POSTPARTUM RISK FACTORS:

These factors include cesarean section (especially emergent CS), medical comorbidities (e.g., varicose veins, cardiac disease, and inflammatory bowel disease), BMI ≥ 25 kg/m², young gestational age (i.e., preterm delivery <36 weeks), obstetric hemorrhage, stillbirth Increased maternal age ≥ 35 years, hypertension, smoking, eclampsia or preeclampsia, postpartum infection, transfusions, and thrombophilia disorders.

• Clinical presentation:

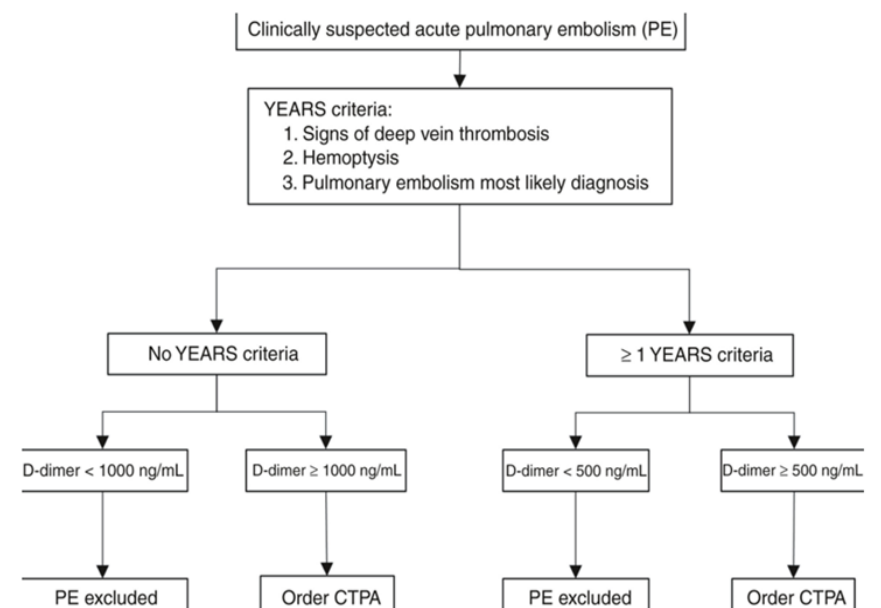
The signs and symptoms of embolism in pregnant women are the same as those in non-pregnant people, which include the sudden onset of dyspnea, pleuritic chest pain, hemoptysis, sweating, and cough. In pregnancy, a series of symptoms can sometimes mimic the symptoms of pulmonary embolism due to the physiological changes in the body of pregnant women. Dyspnea is present in %70 of the pregnant women.

Oxygen saturation in the pregnant women with pulmonary embolism may be normal and does not rule out the pulmonary embolism in any way.

• Laboratory findings:

It is non-specific, but respiratory alkalosis and hypoxia are mainly seen in pulmonary embolism. D-dimer, which is created as a result of breaking blood clots, increases, but the possibility of an amount below 500 ng/dl of VTE is low.

(continued on next page)





(Dr. Leila Namvar Cont.)

• Diagnose:

Traditionally, clinical decision rules such as the Wells or revised Geneva scoring systems have had limited value during a pregnancy. High prevalence of baseline tachycardia.

Revised Geneva score or YEARS criteria: clinical signs of deep venous thrombosis [DVT], hemoptysis PE as the most likely diagnosis

• Treatment:

Application of heparin and enoxaparin is safe in pregnancy. Oral drugs such as warfarin and direct oral anticoagulant (e.g., apixaban, rivaroxaban) are conerindicated in pregnancy. Heparin should be discontinued 36h before a delivery, and anticoagulation should be started 12 hours and six hours later in cases of cesarean delivery and normal delivery, respectively. After delivery, warfarin could be started for the patient and should be accompanied by heparin for five days, and in case of two INR between 3-2 can be discharged.

• NOTE: Application of oral anticoagulants that directly inhibit factor ten (e.g., apixaban and rivaroxaban) is conerindicated during the breastfeeding.

• Duration of treatment:

Minimum of three months. Patients were evaluated for possible continued or indefinite therapy (e.g., persistent risk factors).

Thyrototoxicosis in pregnancy

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Thyroid disorders constitute one of the most common endocrine disorders in pregnancy and occur in about 4% of all pregnancies, with primary hypothyroidism being the most common. Overt thyrotoxicosis can affect between 0.2% and 0.4% of pregnancies, although the prevalence of subclinical thyrotoxicosis can be as high as 1% .The major changes in thyroid function during pregnancy are:

An increase in serum thyroxin-binding globulin (TBG), Stimulation of the thyrotropin (thyroid-stimulating hormone [TSH]) receptor by human chorionic gonadotropin (hCG). It is important to recognize that the standard values of TSH are shifted downward in pregnancy. The first trimester 5th percentile TSH was 0.1 mIU/L and the second trimester was 0.39 mIU/L. These lower values correspond with the peak hCG levels that occur between weeks 8–11 . The decrease in the lower reference limit of TSH in the first trimester is due to human chorionic gonadotropin. In contrast to TSH, thyroxine-binding globulin (TBG) levels increase during pregnancy and peak at approximately 16–20 weeks. With the rise in TBG, total hormone levels also increase .Trimester-specific reference ranges :Weeks 7 to 12 : Reduce the lower limit of the reference range of TSH by approximately 0.4 mU/L and the upper limit by 0.5 mU/L (corresponding to a TSH reference range of approximately 0.1 to 4 mU/L).Second and third trimester : There should be a gradual return of TSH towards the nonpregnant normal range. At approximately 16 weeks, total T4 (and T3) levels during pregnancy are 1.5-fold higher than in nonpregnant women (due to TBG excess). Common cause of Thyrotoxicosis in Pregnancy are GTT and Graves' disease,If a cause of thyrotoxicosis other than GTT is suspected,TRAb levels, thyroid ultrasonography, or the TT3/TT4 ratio may be helpful. The TT3/TT4 ratio is typically >20 incases of overproduction such as Graves' disease and <20 in cases such as thyroiditis. GTT is selflimited and there is no symptoms of hyperthyroidism prior to pregnancy,symptom onset is in the first trimester and there is no family history of Graves' disease and typically there is minimal or absent signs of hyperthyroidism. During the physical exam, there is no evidence of ophthalmopathy, dermopathy (pretibial myxedema), goiter, or Graves' acropachy. thyroid hyperfunction subside as hCG production falls (typically 14 to 18 weeks gestation).Supportive care is all that is typically needed. Short courses of beta-blockers can be used for symptomatic relief if needed. It is reasonable to repeat thyroid levels in 4

weeks. Women with persistent vomiting, significant weight loss, and presence of ketones in urine, hospitalization is very frequently required. Graves' disease is the most common cause of hyperthyroidism in all populations. The course of hyperthyroidism due to Graves' disease tends to improve during pregnancy because of three independent factors: (1) Immunosuppression related to pregnancy tends to decrease production of TRAbs (2) Increased TBG and reduced free thyroid hormone concentrations (3) In iodine restricted areas, increased iodine demand along with decreased supply blunts excessive production. This being said, not everyone is protected from hyperthyroidism by these changes . Management Options for Patients with Graves' Disease are radio iodine,anti thyroid drugs and thyroidectomy. Raidio iodine is Contraindicated in pregnancy, Exposure during thyroid development, from 10 weeks of gestation onwards, will result in fetal hypothyroidism and fetal thyroid ablation needing lifelong thyroxine.Anti thyroid therapy is the firs choice for graves disease in pregnancy.American Thyroid Association guidelines recommend PTU through 16 weeks' gestation and they cite insufficient evidence to recommend switching back. The goal of treatment during pregnancy is to maintain free T4 at maximum normal or total hormones 1.5 times normal by giving the minimum dose of drugs. Thyroidectomy is a treatment option for the management of Graves' disease during pregnancy, but it is typically the last resort due to the associated maternal and fetal risks.Indications for thyroidectomy in pregnancy are Agranulocytosis or hepatotoxicity with ATDs Failure to control thyrotoxicosis despite high dose of ATDs. Anaphylactic or severe allergic reactions to ATDs. PTU and MMI are secreted in breast milk at very low levels .Breastfeeding is safe if the daily dose of PTU or MMI is less than 450 mg or 20 mg/day, respectively, and thyroid function testing of infants is not required.

The Global Landscape of Ischemic Stroke Research

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Worldwide, stroke ranks as the second most common cause of death. Up to %50 of stroke survivors experience chronic disability, which has serious ramifications for both the general public's health and the economy. In the United States of America (USA), 7.6 million people aged 20 years or older had a diagnosis of stroke between 2015 and 2018, with ischemic stroke accounting for %87 of cases. Ischemic strokes can also be classified as non-lacunar or lacunar infarcts, with the latter grouping further into subgroups such cardioembolic, cryptogenic, or main artery blockage. The precise cause of ischemic strokes is still unknown in approximately %17 of individuals.

Scientometrics is a new branch that evaluates and measures scientific literature and in a specific field, it can be used to measure the influence of authors, organizations or even countries. This can have an impact on the direction and policies involved in a field at different levels and help to avoid waste of money, time and resources by making more targeted and accurate decisions and design more accurate researches. Therefore, in this article, we intend to summarize the findings of a recent study that examined the global production of research in the field of stroke with special attention to regional variations, gender differences among authors, subtopics of stroke, and international research collaborations.

All publications reviewed in this paper were extracted from the Web of Science Core Collection along with all relevant metadata up to 2020, with no restrictions on language or country of publication, and finally, after removing unstable data, 21,115 articles were included for the final analysis.

Of these, African authors have published 180 articles, Asia 7644 articles, Europe 7343 articles, Latin American 290 articles, North America 5221 articles, and Australia 437 articles. In total, 132 countries have participated in this issue so far, with the United States producing the most publications (4,614 or %21.9), followed by China with %18.3) 3,872) and Germany with 1,120

%5.3)). They have up to the third in this area.

The H-index and citations show that the United States with H-index 202, Germany with H-index 135 and England with H-index 129 are ranked first to third in the field of publications related to stroke in the case of evaluating the scientific quality of different countries using the H-index method. Compared to the average number of citations per journal, the UK with an average of (50.27), Canada (49.35) and Germany (49.28) rank first to third.

Over time, there is a significant increase in the number of publications in the field of stroke. Among the 21,115 articles, 829 articles were published until 2000, which accounts for approximately %4 of all articles. The rest of the articles, which were 3942, were published between 2000 and 2010. Therefore, the majority of 16,345 of the total 21,115 articles or %77.4 were published after 2010.

%32.3 of the first authors of articles in the field of stroke were women and %67.7 were men. The countries with the highest percentage of female authors among the 20 countries with the highest number of publications on stroke were Poland (%49.8), the Netherlands (%53.4), and Russia (%54.3). Conversely, the countries with the lowest percentage of women were Switzerland (%26.1), Germany (%18.8) and Japan (%14.7).

Overall, the results of this study showed that research on ischemic strokes has increased significantly over time. The topic of ischemic stroke has many connections with cardiovascular medicine, which is particularly evident in the search for underlying causes. Also, the results of this study showed that this scientific perspective is essentially male, especially among the recent authors, and international collaborations around the world play an essential role in ischemic stroke research.

Novel Therapies in the treatment of Diabetic Kidney Disease

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Diabetic kidney disease (DKD) is a chronic kidney disease (CKD) caused by diabetes mellitus (DM). Its pathogenesis is complex and is characterized by increased excretion of persistent albuminuria and, or progressive decrease of glomerular filtration rate (GFR), which eventually develops into end-stage renal disease (ESRD).Diabetic nephropathy (DN) may be a common complication generally seen together in type 1 and type 2 diabetes. Nowadays, in the wake of the increasing prevalence of diabetes worldwide, the incidence of DKD incidence is also rising, which has become the leading cause of ESRD. About %50–30 of the global ESRD is caused by DKD. The occurrence and development of DKD have always been a serious clinical problem that leads to the increase of morbidity and mortality and the severe damage to the quality of life. Controlling blood glucose, blood pressure, blood lipids, and improving lifestyle can help slow the progress of DKD. In recent years, with the extensive research on the pathological mechanism and molecular mechanism of DKD, there were introduced more and more new drugs based on this, with good efficacy in clinical treatment. Clinical trials data have confirmed that early intensive blood glucose control can not only make the blood glucose level reach or close to normal, but also delay the occurrence and development of microalbuminuria and the decrease of estimated glomerular filtration rate (eGFR) in DM patients to a certain extent, and protect renal function. But noticed that about %20 of people with DM developed DKD even if blood glucose is well controlled. Treatment strategies for the management of DN include (a) intensive blood glucose control; (b) attainment of blood pressure goals with the inclusion of angiotensin II receptor blockers (ARBs) or angiotensin-converting enzyme (ACE)-inhibitors in the pharmacologic regimen; (c) weight management with dietary caloric restriction and aerobic physical exercise; (d) dietary protein restriction; (e) smoking cessation; (f) lipid management with statin therapy as the preferred choice; and (g) avoidance of nephrotoxic drugs such as contrast agents, antibiotics, (continued on next page)

(Dr. Farahnoosh Farnood Cont.)

and nonsteroidal anti-inflammatory drugs (NSAIDs) In recent years, the development of new hypoglycemic drugs has dramatically enriched the therapeutic options available for treating T2DM. Notably, some of these new agents, such as SGLT2is and GLP1-Ras, not only mitigate hyperglycemia but also reduce cardiovascular complications and protect kidney function. Although insulin is the only medication available for subjects with T1DM, some of the innovative antidiabetic drugs used approved for T2DM have also shown some beneficial effects in T1DM. From the category of new drugs for diabetes, we can mention the following:

GLP1- receptor agonists have shown beneficial effects on diabetic nephropathy (DN) by protecting the kidneys and improving renal outcomes. They have been found to have anti-inflammatory and antifibrotic effects in the kidney, which contribute to kidney protection .GLP1- receptor agonists increase GLP1- receptor (GLP1-R) expression and attenuate the upregulation of receptor for advanced glycation end products (RAGE) in the presence of advanced glycation end products (AGE), leading to improved cell viability .Liraglutide, a GLP1- receptor agonist, has been shown to inhibit inflammation and oxidative stress, reduce urinary albumin excretion, and protect podocytes in DN patients .GLP1- receptor agonists confer kidney protection through indirect effects such as improvement of blood pressure, glycemic control, and weight loss, as well as direct effects including restoration of normal intrarenal hemodynamics and prevention of ischemic and oxidative damage .The renoprotective mechanisms of GLP1- receptor agonists include inhibition of oxidative stress and inflammation, as well as induction of natriuresis through their pleiotropic actions.

They improve renal tubular function and increase natriuresis and diuresis. The effect of GLP1-RAs on renal hemodynamics is ascribed to the improved equilibrium between afferent vasodilation and efferent vasoconstriction .The tubular transporter most likely mediating the natriuretic effects of GLP1- is the sodium–hydrogen antiporter, also known as sodium hydrogen exchanger 3 (NHE3), which is found on the edge of the brush of the proximal tubule. NHE3 is inhibited by decreased postprandial levels of glucagon insulin or glucose, which leads to downregulation and inhibition of NHE3. Interestingly, beyond the endocrine pancreas, GLP1- receptor mRNA has been localized in the central and peripheral nervous systems, gastrointestinal tract, cardiovascular system, kidneys, and lungs .Therefore, it is plausible to assume that, in addition to their glucose-lowering actions, these drugs have anti-inflammatory and antioxidant effects which could directly or indirectly improve kidney function.

The next group of drugs are simultaneous inhibitors of sodium and glucose. This group of drugs are sodium-glucose cotransporter2- (SGLT2) inhibitors, which cause the excretion of glucose from the urine. These drugs were initially approved to reduce glycosylated hemoglobin (HbA1c) in patients with type 2 diabetes, but later it was found that these drugs reduced the risk of hospitalization due to heart failure and the progression of chronic kidney disease (CKD).) in high-risk patients.

Despite the significant advantages mentioned, the physiological mechanisms of this class of drugs are incompletely understood. SGLT2 inhibitors stimulate osmotic diuresis and transiently cause sodium excretion. This happens in the use of other diuretics as well, but the key difference between this group of drugs and other conventional diuretics is the specific reduction of the extracellular volume without affecting the blood plasma volume.

Future considerations in the treatment of this category of patients include the use of cell-free therapies, for example, the use of MSC derivatives such as extracellular vesicles Cytokines and growth factors that have less immune effects than MSCs. But it should be noted that in this context ,The method of tissue harvesting, isolation and growth of MSC is still challenging, but these technologies are promising for treatment. Therefore, in the coming years, we should expect new therapeutic strategies for the targeted treatment of patients with diabetic nephropathy.

The Stem Cell Transplantation strategy

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The important factors in SCT are donor, graft and conditioning regime. And I describe these important factors in this lecture.

Hematopoietic stem cell transplantation divided into categories, A key component of the decision-making process of transplantation is selection of the appropriate donor and graft. When graft is from the patient himself it is named autologous transplantation. Hematopoietic progenitor cells to support hematopoietic recovery after high dose chemotherapy has revolutionized transplantation for a variety of disease. In allogenic stem cell transplantation, the best donor is an HLA-matched sibling, however this option is available only for one third of patients While the choice of a graft type is often determined by the transplant center preference and experience. Initial allogenic transplants were done using bone marrow grafts. More options are currently available:

- 1.Peripheral blood
- 2.Bone marrow
- 3.UCB

Stem cell transplantation has rapidly expanded in scope, practice and basic understanding in the past 20 years. The indications now encompass a wide and diverse range of disease include autoimmune disease such as MS and Scleroderma. Conditioning therapies of varying intensities and numerous strategies with novel cells, processed cells and genetically re-engineered products. Combination of these cell therapies decrease SCT complications. Hematopoietic stem cell transplantation (SCT) is an established curative treatment for a number of conditions including: malignant disease and nonmalignant congenital and required disease. The number of transplantation has steadily increased since 2000.

The annual number of unrelated donor transplants has increased in 2011 and the number of unrelated SCT, bone marrow as a graft source decreased in favor of peripheral blood. Within the last few years, a trend towards alternative donors has been noted. Improvements in techniques leading to better patient and donor selection, the use of reduce intensity conditioning regimens, and improvement in supportive care are likely contributors to age trends among SCT recipients. Haploidentical transplantation perform about all patients.

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