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本期封面: **Sedona, Arizona** 王 清 摄影作品

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尊敬的读者:

感谢您正在阅读本期CASA协会的刊物。鉴于本刊并未设定同行评审 (peer review) 机制, 于本刊所投及发表的学术文章可仍于今后发于Peer Review刊物。已正式发表的文章亦可于本刊物转载。本编辑部鼓励专业同行积极投稿, 为我们麻醉事业的发展努力。

We appreciate your attention to this issue of CASA's publication. As this journal does not employ a peer review process, academic articles submitted and published in this journal retain the potential for future publication in peer-reviewed journals. Additionally, officially published articles may be reprinted in this journal. The editorial board strongly encourages our colleagues to actively submit articles and contribute to the advancement of anesthesiology.

本期导读

本期的会员游记刊登了编辑申建成最近在曲阜的有趣经历。

POCUS最近在麻醉的临床应用越来越广泛，已经成为了住院医师培训的重要组成部分。可是对于很多之前毕业的麻醉医生来说，可能还有些陌生。前会长汪红教授是该领域的专家，经常担任多个培训班的指导老师。本期刊登了汪教授在最近在ASA POCUS workshop所使用的handout。

本刊编辑蒋天宇根据前会长李金蕾最近发表的关于脊髓麻醉的综述撰写了文献速递。

随着钠葡萄糖偶联运输蛋白二型抑制剂（SGLT-2i）的越来越广泛的应用，为我们的日常麻醉管理提出了新的挑战。前会长曹锡清为本刊特别撰写了关于围术期管理的综述，包括

是否需要停药，停药时长，以及如果未停药应当如何应对，并且分享了所在医院系统的处置方案。

CASA前会长Henry Liu为本刊特别撰写了介绍一氧化氮(NO)和心血管健康的综述。探讨了一氧化氮的合成和机理，在心血管疾病中的作用，以及在其基础上研发的药物和方向。

本期的最后依然是我们敬爱的CASA创始人之一王海明医生的回忆录。其中介绍了CASA的成立过程，以及很多前辈对CASA的成长做出的卓越贡献。

本期封面及插图均是来自于我们CASA前会长王清的摄影作品。



(王清摄影作品，Yosemite Falls, Yosemite National Park)

曲阜游记（申建成 医生）

二十多岁时爬过两次泰山,没有去邻近的曲阜,知道曲阜是孔子故里,那时对孔子的了解和尊敬非常有限。

听说孔子源于“批林批孔”,当时我还在上小学,老师和广播里说,坏人林彪一家叛国投敌,摔死在温都尔汗。毛主席说批判林彪时也要批“孔老二”,批“孔孟之道”,那就是轰轰烈烈的“批林批孔”运动。记得是这样说的,“孔老二”叫孔丘,家里排行第二,生于春秋时代的鲁国,当过小官,周游列国,传播反动思想,要“克己复礼”。他和林彪一样,会让我们回到万恶的旧社会,吃二遍苦,受二茬罪。

毛泽东去世后,不说“孔老二”了,改称孔子,但先入为主,总觉得孔子只是中国一个有争议的历史人物。后来去荷兰工作,上班第一天,一个同事跑来问我,你从中国来,肯定知道“Confucius”了,我没听懂,说不知道,他盯着我连说了几遍 Confucius,说你一定知道,另个同事帮腔解释,才搞清楚,说的是孔夫子。

很吃惊老外们都知道孔子,看来孔夫子在世界上也很有名,为什么中国人自己要和他过不去呢?

渐渐知道了,孔子是中国古代最著名的教育家和思想家,是传统儒学的奠基人,两千年前就提出了“有教无类;因材施教;温故知新”,这样先进的教育思想,和“中庸,仁,义,礼,智,信,孝,悌,忠,恕”等普适的思想理念。孔子是世界教科文组织首位介绍的人类历史文化名人,和他并列的还有,耶稣,释迦牟尼,穆哈默德,亚里士多德.....。

孔子和他的门生们创立的儒家思想曾是中国延续了两千年的主流意识形态,也深刻影响了日本,朝鲜,越南等中亚文化圈的思想。

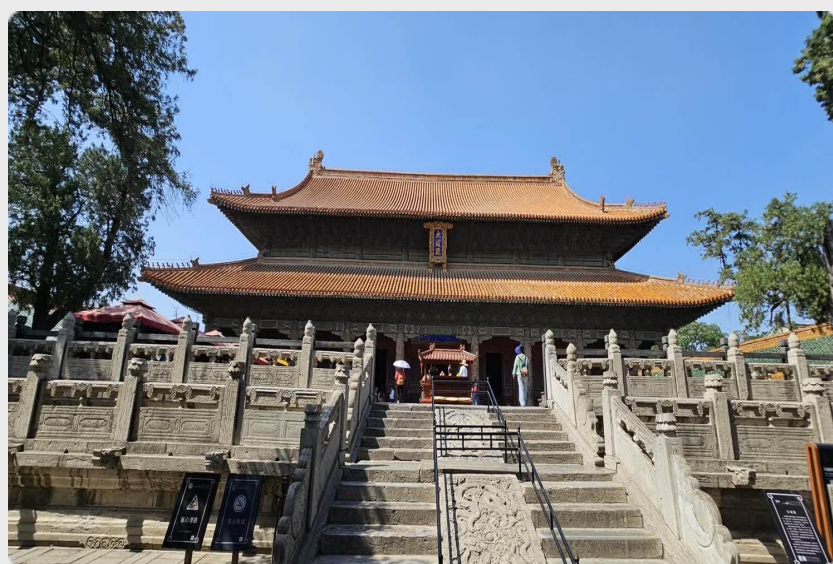
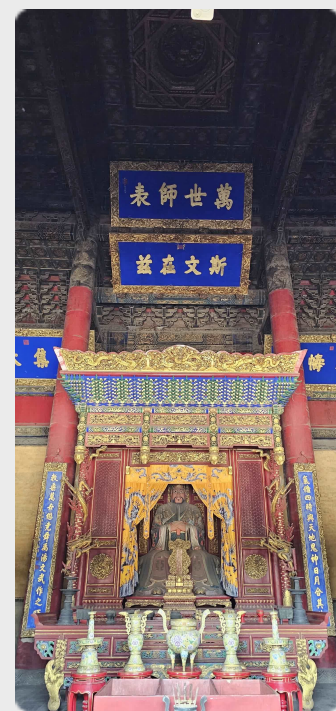
秦始皇不喜欢儒家,残酷地焚书坑儒,秦朝二世而亡。之后两千年,每朝每代都把儒学做为立国之本,把孔子奉为万世

师表。包括蒙古族统治的元朝,满族的清朝,都把孔子尊为圣人,当做道德文化的核心。

儒家的四书五经,更是科举考试的教科书和经典文本,“学而优择士”,儒学是平民入官的必修课。

这次回国终于有机会来到曲阜,亲眼看看孔子故里,了却一个很久的愿望。

孔子故里历经千年,经过无数个皇帝的彰显和加持,逐渐形成了孔庙,孔府和孔林三大文化奇观。孔庙是仅次于故宫,承德避暑山庄的中国第三大古建筑群。有康熙题字的万仞宫墙,历代题字碑,故宫里也找不到的雕龙石柱,雄伟的大成殿,多位皇帝书写的匾额,巨大的藏书楼,数不尽的古柏和道不完的故事。



儒家思想在中国封建社会中渗透了政治,道德和伦理的方方面面,近代有人认为儒家学说如“三纲五常,君君,臣臣,父父,子子.....”中的糟粕部份禁锢了人们的思想和行为,应该让位于新思想,更有人想把它彻底铲除掉。

文革中北京的红卫兵响应毛主席“破四旧”号召来到曲阜，他们要捣毁封建主义的老巢----孔家店。红卫兵造成了孔庙历史上最严重的人为破坏，题字碑几乎都被推倒损坏，无数典籍文物被焚毁，孔子塑像被打碎，孔林里的很多坟墓被掘开。



孔府是孔子嫡长孙，世袭“衍圣公”的府邸，是他们的世代居住地。四九年孔子第七十六代孙孔德成跟随国民党去了台湾。他若留下，可以想见文革中会发生什么。庆幸的是传统

文化经过几十年的震荡终又回归，零八年孔德成去世后得以归葬曲阜孔林，之后的孔家嫡长孙还会回到孔府生活吗？

一个千年思想不可能没有脱离时代的东西，它毕竟是中国漫长历史一个重要组成部份，不应人为割裂，怎样留下它的精华，考验着现代人的智慧。在孔府里看到一株被雷电劈成六瓣的古柏，仍然顽强地活着，中心还长出了一棵生机勃勃的新树苗，这不正是儒学等中国传统思想的今天吗？

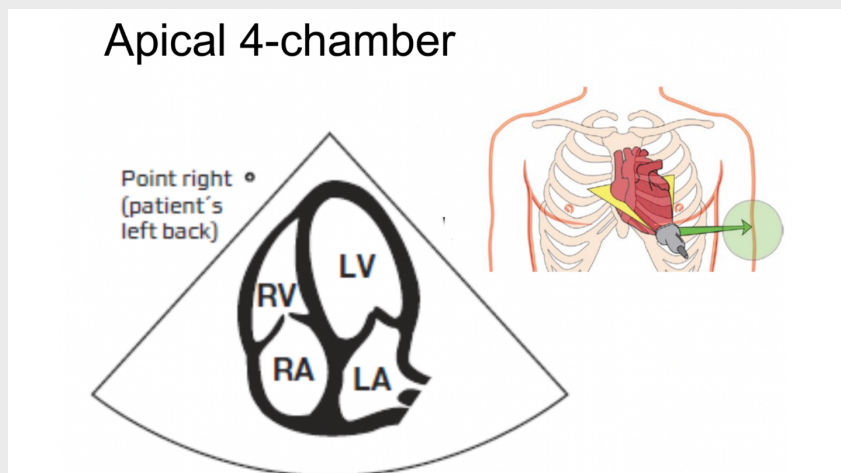
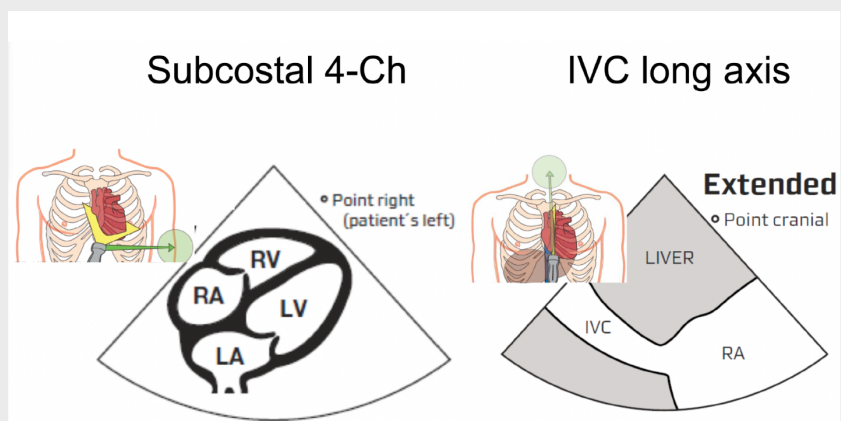
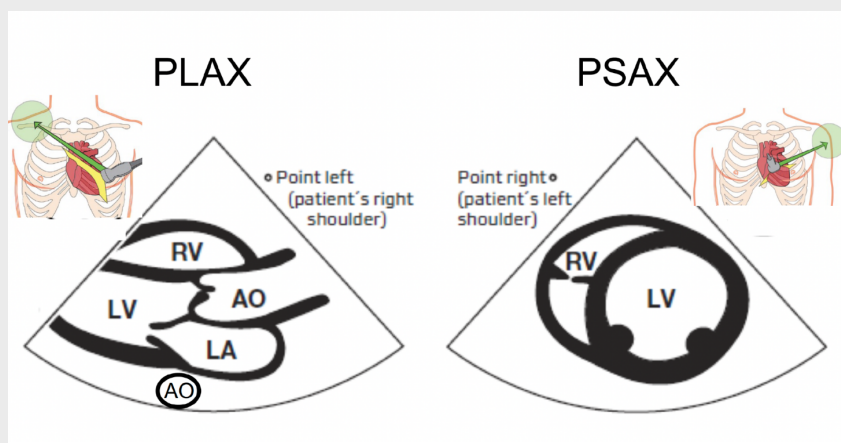
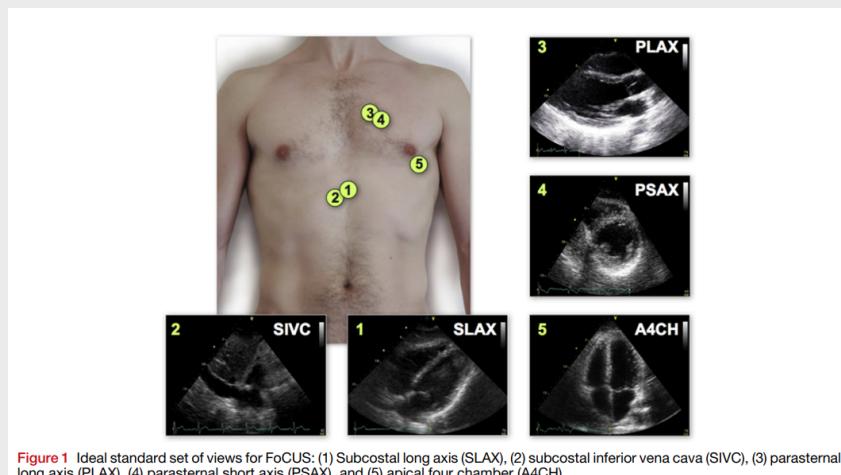
申建成

Sacramento, California

2025.06.12



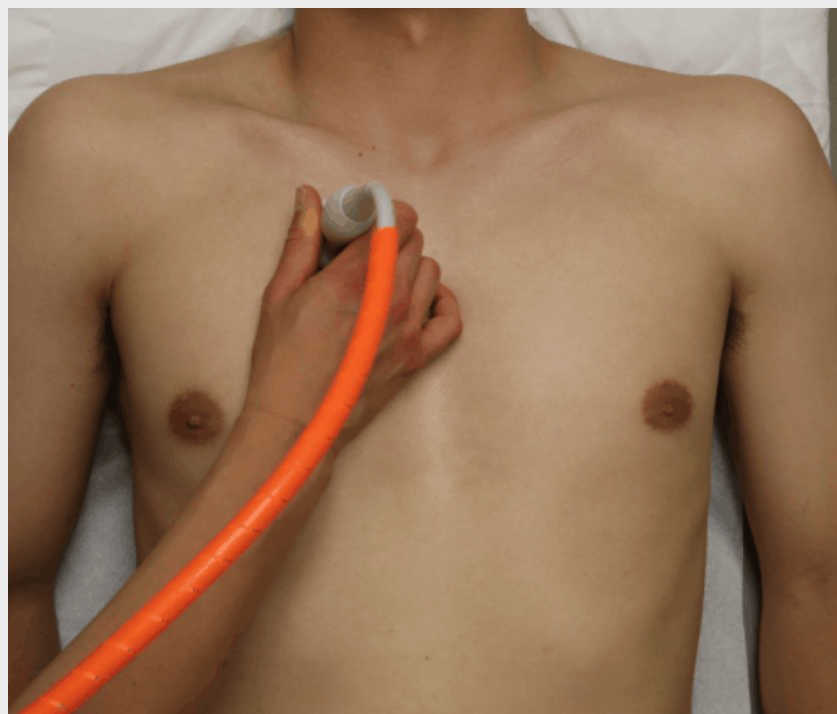
2025 ASA POCUS Workshop Handout (汪红 撰稿)



Lung Ultrasound of ANTERIOR Chest

Point 1 (R1 and L1) assesses the anterior chest. This point will be most relevant when assessing for **pneumothorax** and/or **interstitial edema**.

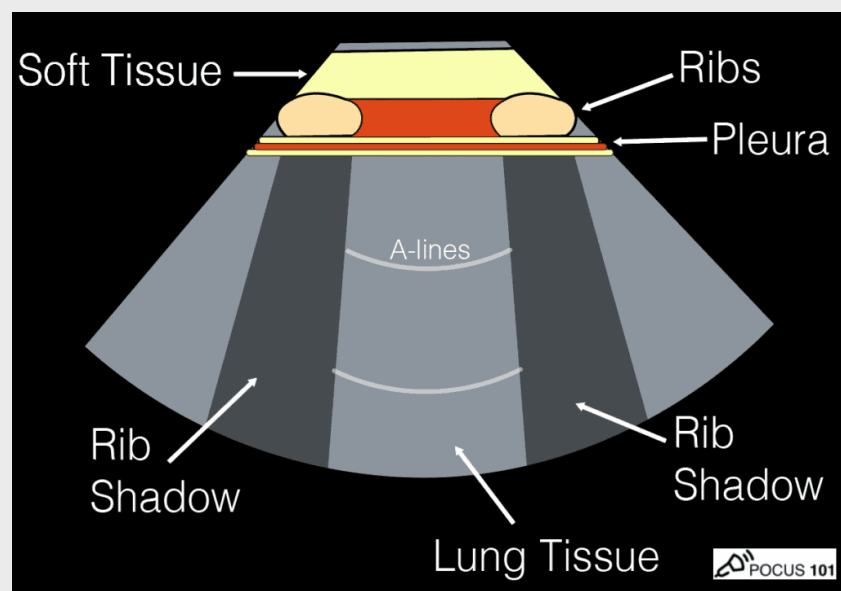
- Point your indicator towards the patient's head.
- Place your probe at the **mid-clavicular line at the 2nd intercostal space of the right (R1) and left (L1) lungs respectively**
- Anchor your probe in the space between two ribs.



R1 Ultrasound Probe Position

Identify Two Rib Shadows (Batwing Sign)

- The first lung ultrasound finding to confirm you are in the correct position is to look for the two rib shadows or the "**Batwing Sign**." This ensures that your probe is in between two ribs.





Batwing Sign on Ultrasound

Identify Lung Sliding

- The next finding you will want to look for is lung sliding.
- Lung sliding is a normal finding where the visceral and parietal pleura slide back and forth on one another as the patient breathes. Some say this looks like tiny “ants marching on a line.”
- This is a simple finding but extremely useful since lung sliding definitely means that the visceral and parietal pleura are next to each other, effectively ruling out pathology such as pneumothorax.

Editor’s Note: Lung sliding can be seen with the phased array and curvilinear ultrasound probes. However it is often times most easily seen with the linear probe given how shallow it is.



Lung sliding with linear probe

Lung Ultrasound of POSTERIOR Chest

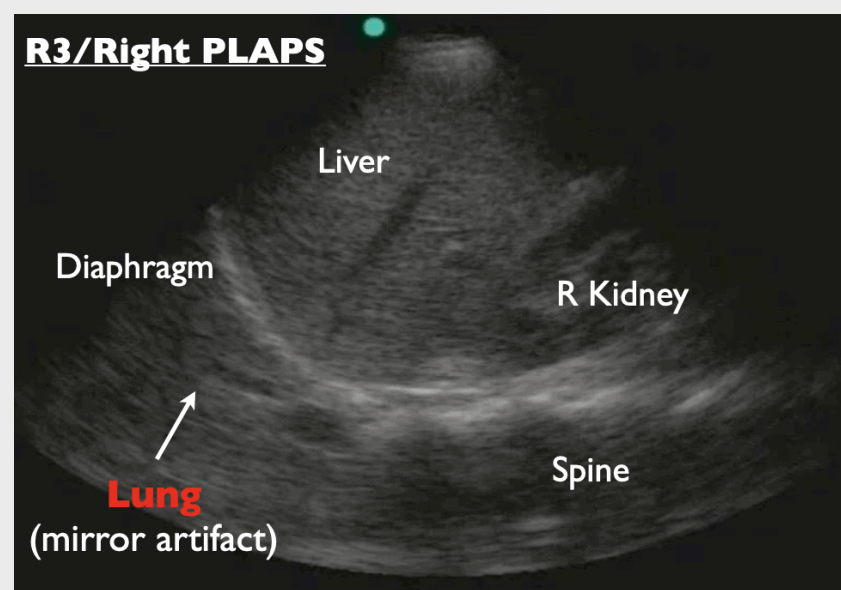
Point 3 (or R3 and L3) assesses the posterior chest. This point is commonly known as the **PLAPS** point on lung ultrasound (“posterior and/or lateral alveolar and/or pleural syndrome”). The PLAPS will be most relevant for assessing the presence of **pleural effusions and consolidations**.

- Point your indicator towards the patient’s head.
- Slide the probe under the patient at the PLAPS point at the **intersection of the posterior axillary line and a rib space between the 10th and 12th ribs**.

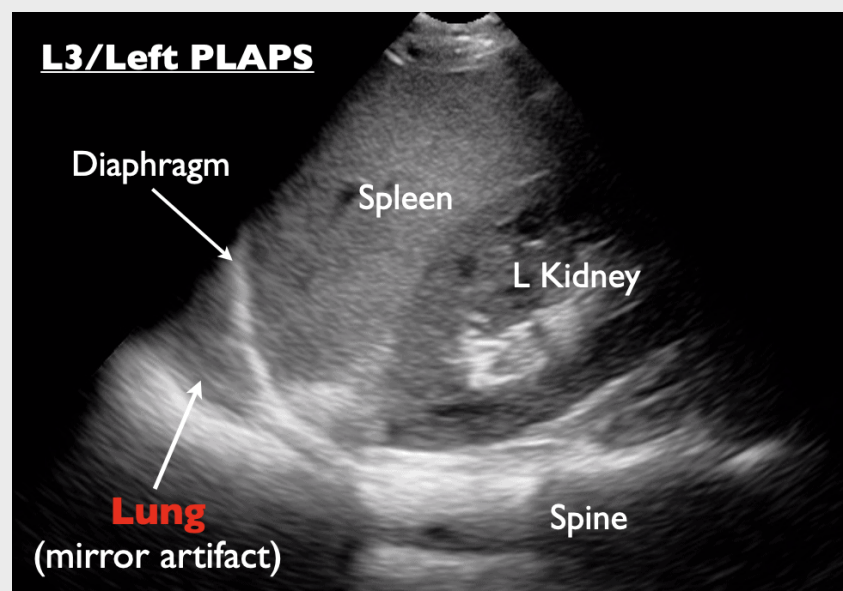


R3 – PLAPS Point

- Identify the **liver** (right side) or **spleen** (left side), **kidney**, and **diaphragm**.
 - These organs will come in and out of view when the lung inflates and deflates.
- You should also see the **spine**, which in healthy lungs, extends up only until the border of the diaphragm. If it extends past the diaphragm called the “spine sign”, you will need to look for a pleural effusion or consolidation which we explain how to do in the pathology section.



R3 (Right PLAPS point)



L3 (Left PLAPS point)

Right Upper Quadrant View (RUQ)

For the right upper quadrant and left upper quadrant views. Remember to look free fluid both above (hemothorax) and below (hemoperitoneum) the diaphragm.

RUQ View: Does my patient have free fluid in the abdomen or right thorax?

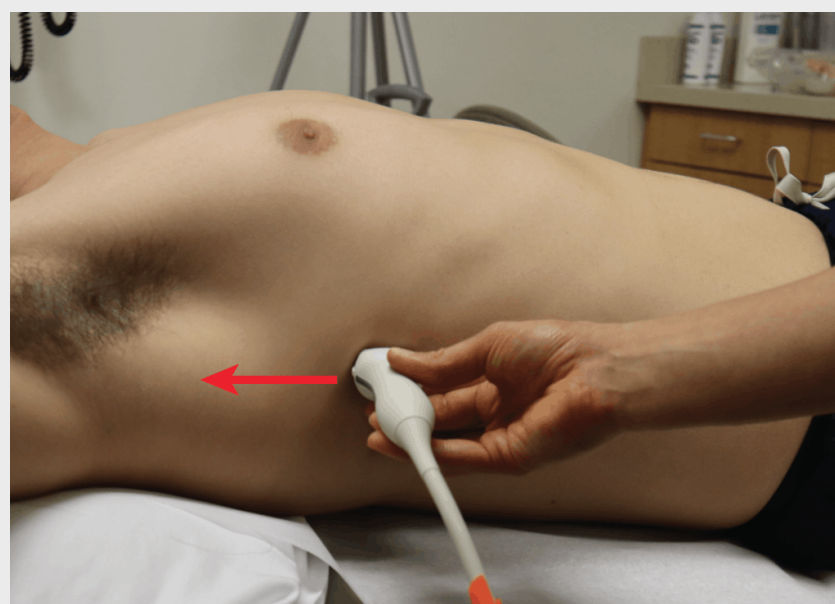
Since the liver is the most commonly injured organ in blunt abdominal trauma, the right upper quadrant is usually the most sensitive view of the eFAST exam.

RUQ Probe Position and Hand Placement

- Orientate the **probe indicator** towards the **patient's head**.
- **Anchor** your probe in the **midaxillary line** at the **10th intercostal space**.



Probe Placement – RUQ

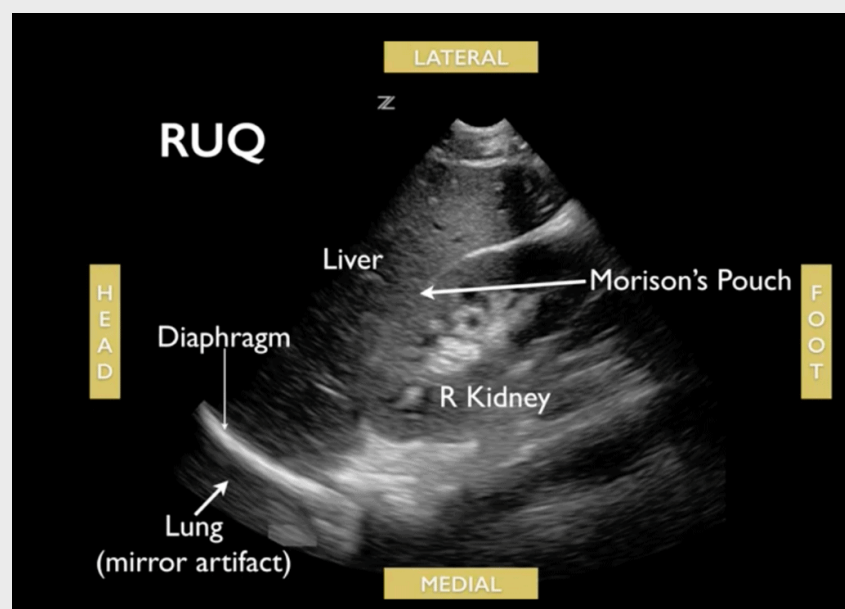


Exam Probe Placement – RUQ

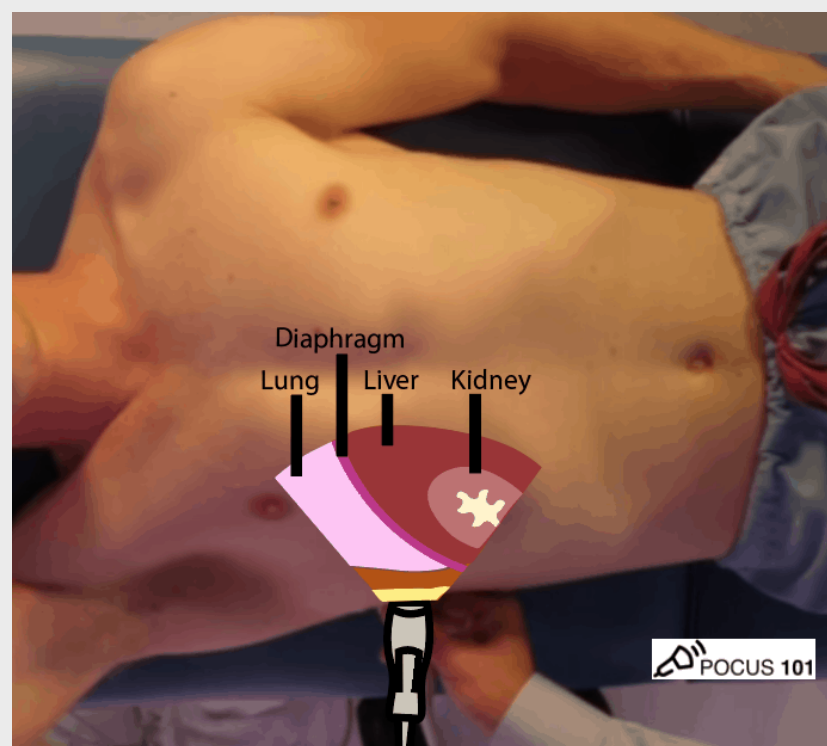
RUQ Normal View and Structures

- Using the *liver as an acoustic window*, identify the **lung**, **liver**, **Morison's Pouch**, **diaphragm**, and the long-axis of the **right kidney**.
- **Morison's Pouch** is where you usually identify free fluid in the RUQ view.
- A Mirror Image Artifact is a normal finding signifying there is an aerated lung above the diaphragm. If you want to dive a little deeper into the physics of the Mirror Image Artifact, [click here](#).

- You may have to **slide up** or **down** a rib space to identify the structures.
- POCUS 101 Tip: these structures move as the diaphragm contracts and relaxes during the respiratory cycle. Consider asking your patient to hold their breath to keep the desired organs from moving. Also, consider slightly rotating the probe counterclockwise towards the bed so that the probe fits better between the rib spaces.*



Normal RUQ exam



RUQ exam illustration

Left Upper Quadrant View (LUQ)

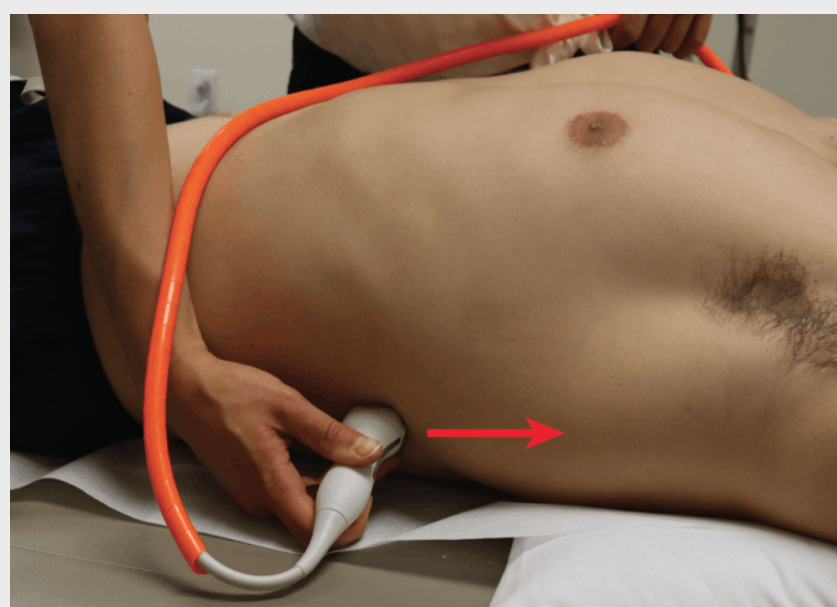
LUQ View: Does my patient have free fluid in the abdomen or left thorax?

LUQ Probe Position and Hand Placement

- Grasp the linear probe between your **thumb** and **first finger**, like holding a pencil.
- Orientate the **probe indicator** towards the **patient's head**.
- Anchor your probe in the **posterior axillary line** around the **8th intercostal space**.
- You should have your "Knuckles to the bed" since the spleen is fairly posterior.



Exam Probe Placement – RUQ

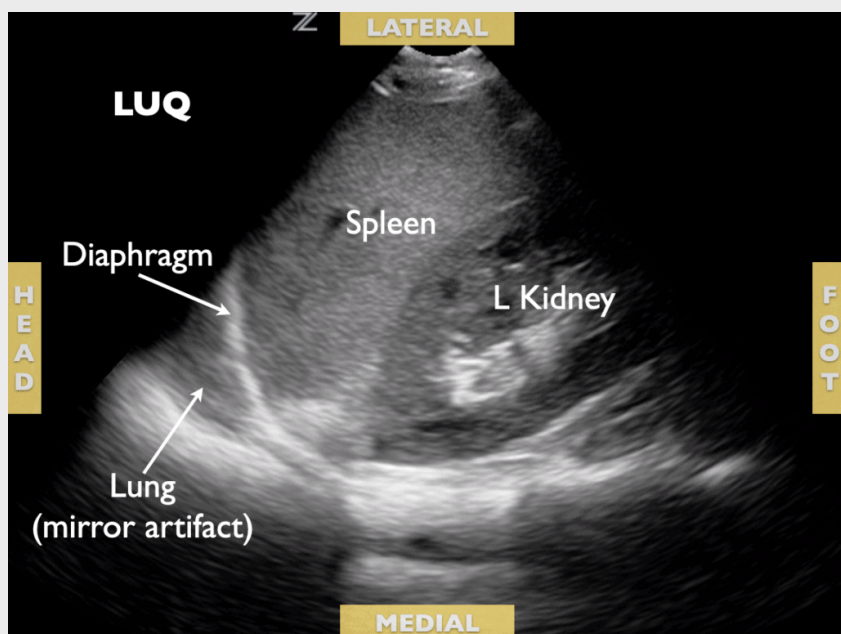


"Knuckles to the Bed" for the LUQ exam view

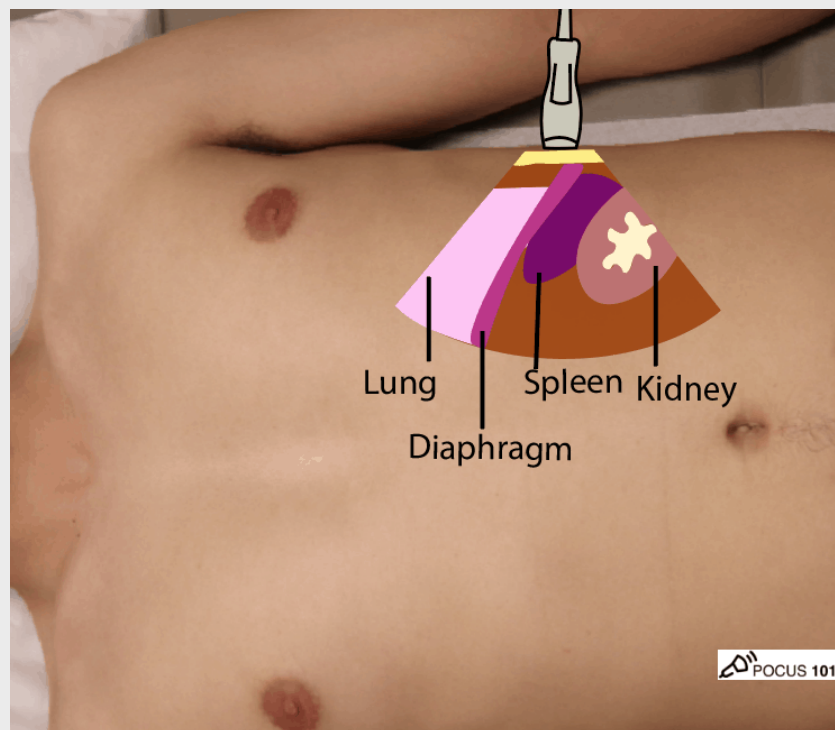
LUQ Normal View and Structures

- Using the *spleen as an acoustic window*, identify the **spleen**, **perisplenic space**, **diaphragm**, and the long-axis view of the **left kidney**.

- Free fluid in the LUQ is most frequently seen in the perisplenic space (between the spleen and the diaphragm). The reason is that there is a splenorenal ligament limiting the ability of fluid to track in between the spleen and left kidney
- A **Mirror Image Artifact** is a normal finding, similar to the RUQ, signifying there is an aerated lung above the diaphragm. If you want to dive a little deeper on this, [see here](#).
- You may have to **move up** or **down** a rib space to identify the structures.
 - *POCUS 101 Tip: these structures move as the diaphragm contracts and relaxes during the respiratory cycle. Consider asking your patient to hold their breath to keep the desired organs from moving. Also, consider slightly rotating the probe clockwise towards the bed, so that the probe fits better between the rib spaces.*



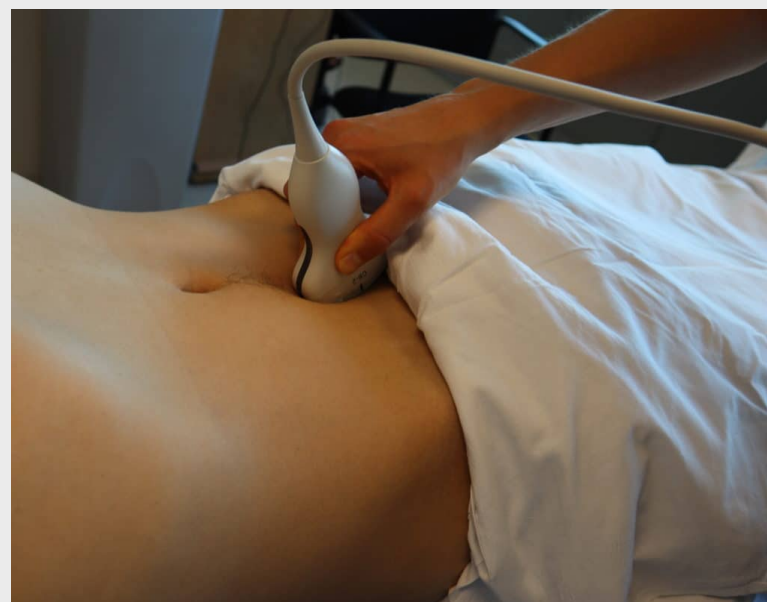
Normal LUQ –exam



LUQ exam illustration

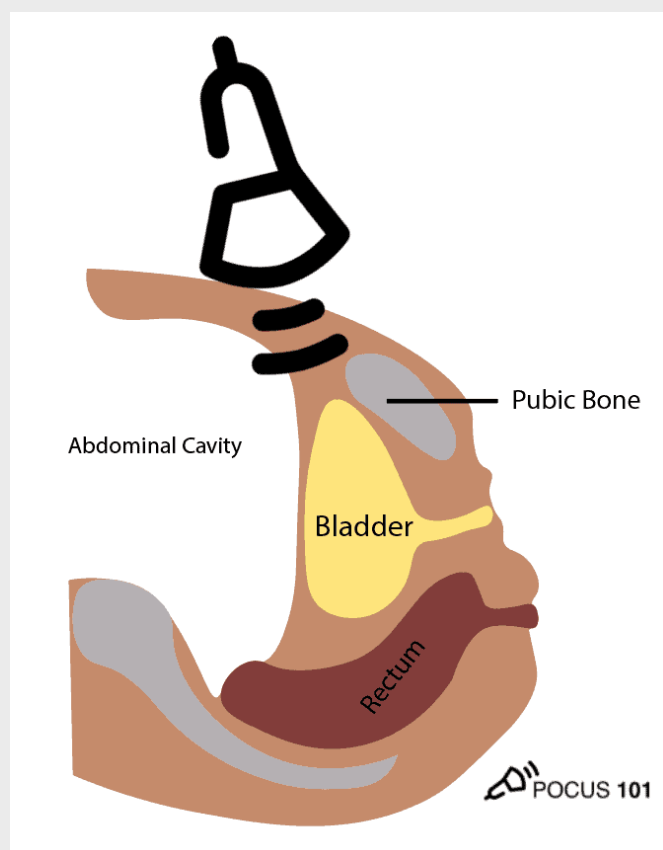
Bladder Ultrasound – Longitudinal View

- Place the transducer with the **indicator pointing towards the patient's head** in the patient's midline, right above the **pubic symphysis**.
- Rock the probe so that it **points down towards the pelvic cavity**.

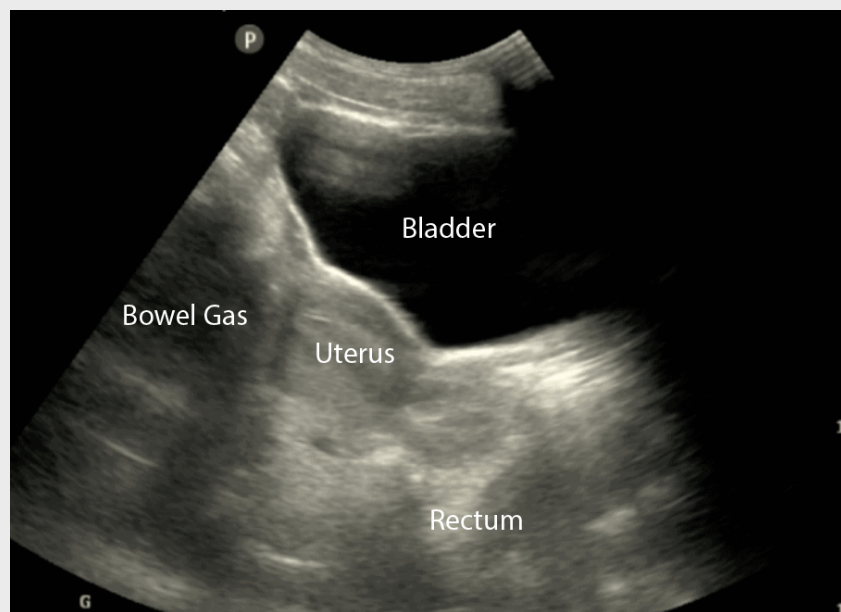


Bladder Ultrasound – Longitudinal View

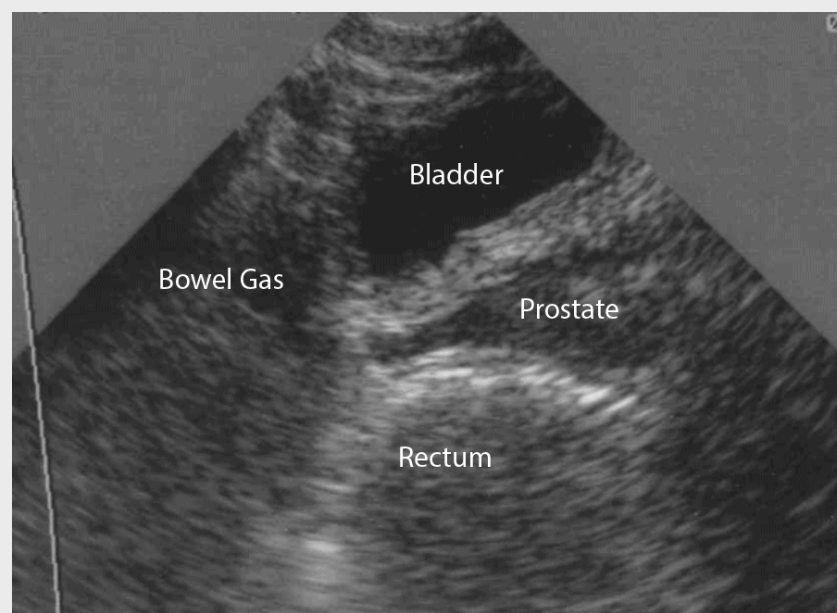
POCUS 101 Tip: One of the most important things to remember when performing bladder ultrasound is that the bladder is directly posterior to the pubic bone/symphysis. If you are unable to get proper images, most likely your ultrasound probe is placed too superiorly.



- In the longitudinal (sagittal) view, identify the **Bladder**, **Bowel Gas**, **Uterus** (females), **Prostate** (males), and **Rectum**.



Female Bladder Ultrasound – Longitudinal View



Male Bladder Ultrasound – Longitudinal View

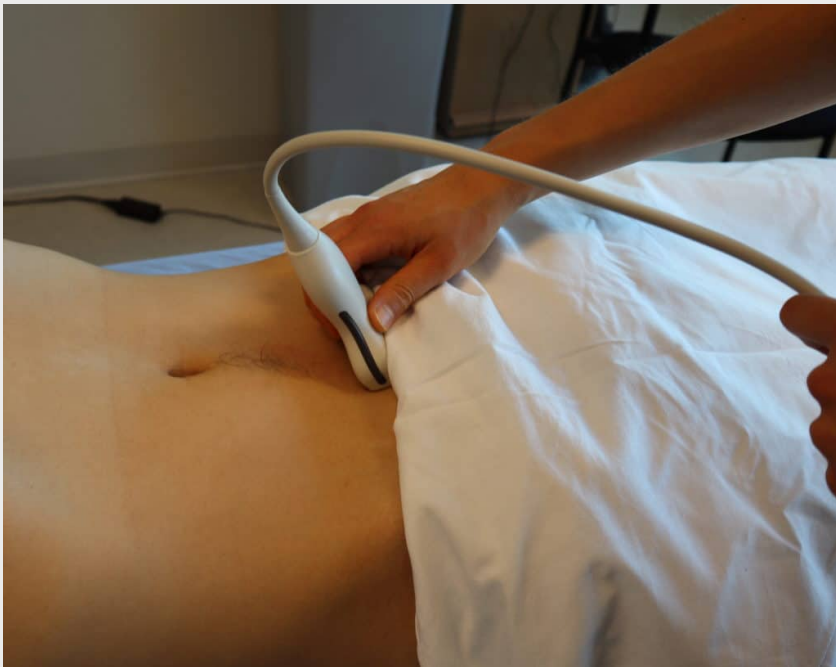
- Observe the lateral borders of the bladder by tilting/fanning the probe left and right.



Tilting the probe in the longitudinal view

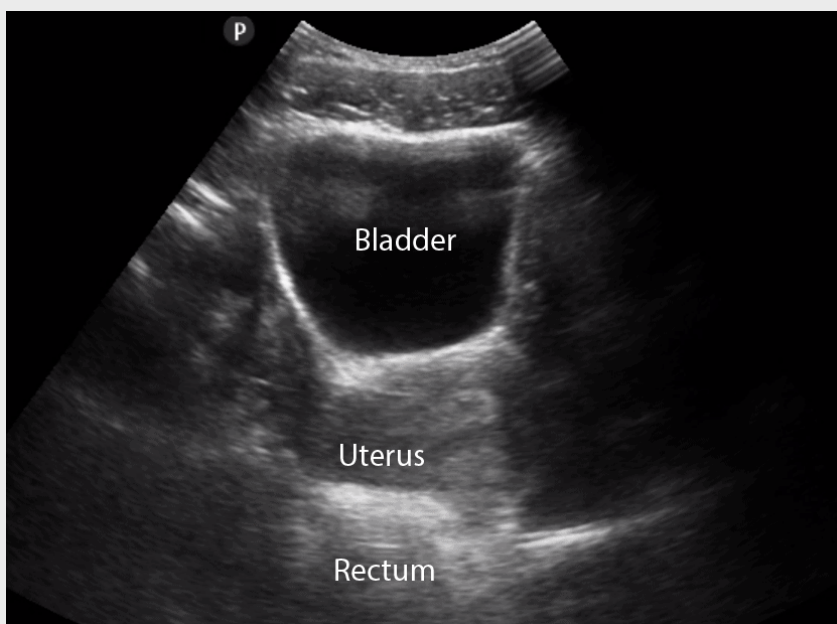
Bladder Ultrasound – Transverse View

- Next, center the bladder and then rotate the transducer **90 degrees counterclockwise**. The indicator should now point to the patient's **Right side**.
- Make sure to tilt the ultrasound probe so it scans into the pelvic cavity.

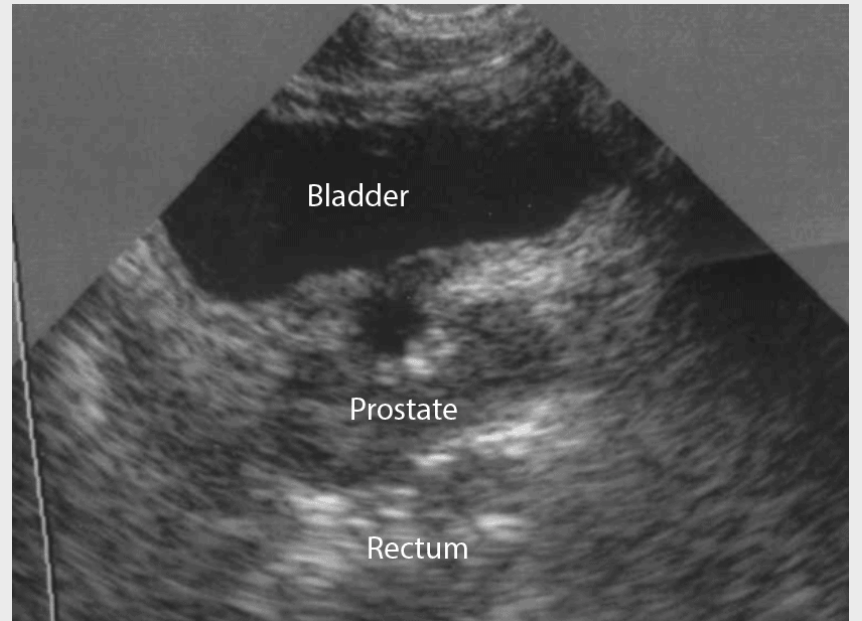


Transverse View

- In the [transverse](#) view, identify the **Bladder**, **Uterus** (females), **Prostate** (males), and **Rectum**.

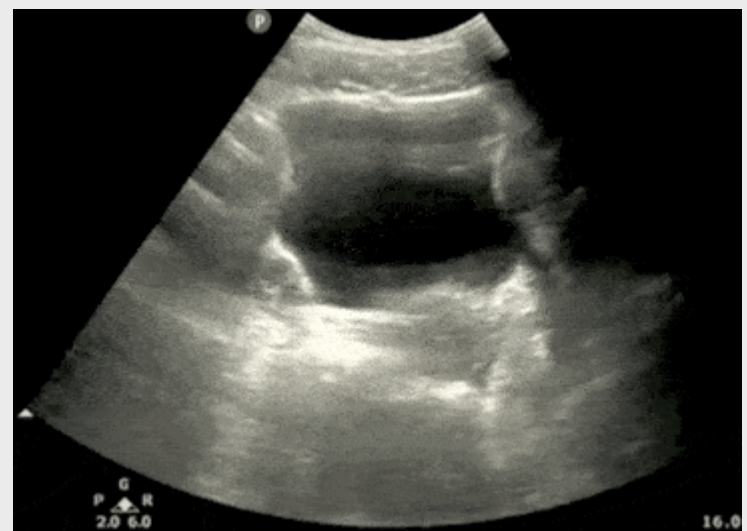


Female Bladder Ultrasound – Transverse View



Male Bladder Ultrasound – Transverse View

- [Tilt/Fan](#) the probe to examine the entire bladder from superior to inferior.



Transverse view of a full bladder

文献速递 (蒋天宇 撰稿)

多模式脊髓麻醉的文献综述

Doris Pierson, Rebecca Certoma, Joshua Hobbs, Xiaomei Cong, Jinlei Li,

A narrative review on multimodal spinal anesthesia: Old technique and new use, *Journal of Anesthesia and Translational Medicine*, Volume 4, Issue 1, 2025, Pages 25-32, <https://doi.org/10.1016/j.jatmed.2025.02.002>.

(<https://www.sciencedirect.com/science/article/pii/S2957391225000075>)

(原文作者为CASA原会长李金蕾医生)

Indication and contraindications

Spinal anesthesia is primarily indicated for surgeries below the umbilicus, including urologic, gynecologic, obstetric, lower abdominal, perineal, lower limb vascular and orthopedic procedures. More recently, it has also been applied to major upper abdominal to provide analgesia below the neck. Absolute contraindications are patient refusal, elevated intracranial pressure, hemodynamic instability, allergy to medications, and infection at the puncture site. Relative contraindications are neurological diseases with variable course (like multiple sclerosis), thrombocytopenia or coagulopathy, and fixed cardiac output states. Spinal anesthesia in immunocompromised patients, those with prior spinal surgery, or HIV requires individualized risk–benefit analysis, but these are no longer considered absolute contraindications.

Spinal techniques

Spinal anesthesia is performed by inserting a needle into the lumbar subarachnoid space, most often at the L3/4 or L4/5 interspace, to deliver local anesthetics. The midline approach is the most common technique. Paramedian approach does offer higher first-pass success rates in older patients and lowers post-

dural puncture headache (PDPH) risk in obstetrics. Ultrasound-assisted or guided spinal anesthesia has become increasingly used to improve accuracy, especially in patients with difficult anatomy. Variations such as unilateral spinal anesthesia, achieved by maintaining lateral decubitus positioning after injection of hyper- or hypobaric agents, allow targeted anesthesia with fewer hemodynamic side effects.

Medications used in spinal anesthesia

Spinal anesthesia uses both local anesthetics and adjuvants. Only 2-chloroprocaine and hyperbaric bupivacaine are FDA approved for spinal use. Adjuvants are added to enhance block quality and duration while reducing anesthetic dose. This includes opioids, $\alpha 2$ -agonists, glucocorticoids, ketamine, magnesium sulfate, and nalbuphine. Each has distinct benefits and side effects—for example, morphine provides long-lasting analgesia but can cause pruritus and respiratory depression, while dexmedetomidine/clonidine extends block duration without pruritus but may cause hypotension and bradycardia.

Complications

Severe complications such as spinal hematoma, meningitis, or nerve root injury, are uncommon. Moderate complications include PDPH and failed spinal block. Mild but frequent problems include nausea, vomiting, shivering, itching, urinary retention, and even transient hearing impairment. While most complications are self-limited or manageable, awareness and prompt management are key to maintaining the safety profile of spinal anesthesia.

Continuous Spinal Anesthesia (CSA)

CSA involves placing an indwelling catheter into the subarachnoid space to allow intermittent or continuous dosing of local anesthetic, providing longer duration and more precise control than single-shot spinal. Use of CSA declined initially due to complications like cauda equina syndrome, especially when using microcatheters and lidocaine. Later reintroductions with better catheter designs showed advantages over single-shot

spinal and epidural anesthesia, including improved hemodynamic stability, lower vasopressor requirements, and more predictable block spread. However, CSA carries risks of technical difficulty, catheter misidentification (as epidural), and dense motor blockade. In US, only standard epidural catheters are used for CSAs.



(王清摄影作品, Badwater, Death Valley National Park)

Original Article（原创文章）

服用SGLT-2抑制剂的日间手术患者是否需要术前停药3-4天

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Sodium-Glucose linked transporter 2 inhibitors (SGLT-2i , 钠葡萄糖偶联运输蛋白二型抑制剂) 亦称gliflozins(格列净), 是2013年由美国FDA批准的一类用于治疗二型糖尿病的药物 (Table 1) ¹。大量近期研究证明患者使用SGLT-2i后临床预后改善包括血糖控制改进，严重并发症例如糖尿病合并的慢性肾病进展延缓，防止糖尿病患者罹患冠心病，心衰复发率降低甚至有益于非糖尿病患者的心衰改善，但是没有降低卒中的发病率。所以近来格列净类药物特别是Empagliflozin (Jardiance) 也被用于治疗慢性肾病，心衰和冠心病²。本文将系统回溯SGLT2i的作用机制包括降糖，降血压和降体重的原理，适应症，对心血管尤其是心衰和慢性肾病的益处，多种副作用，围术期使用此类药物的患者管理。针对2024 AHA/ACC等提出的术前停药3-4天的指南是否对日间手术后可以立即进食的患者有例外，我提出个人意见与大家商榷讨论。

Table 1 :

Sodium-glucose linked transporter 2 (SGLT-2) inhibitors and combinations
<i>SGLT-2 inhibitor</i>
Bexagliflozin
Canagliflozin (Invokana)
Dapagliflozin (Farxiga)
Empagliflozin (Jardiance)
Ertugliflozin (Steglatro)
Sotagliflozin

<i>Combination with dipeptidyl peptidase 4 (DPP-4) inhibitor</i>
Dapagliflozin and saxagliptin
Empagliflozin and linagliptin
Ertugliflozin and sitagliptin
Combination with metformin
Canagliflozin and metformin
Dapagliflozin and metformin
Empagliflozin and metformin
Ertugliflozin and metformin
<i>Combination with a DPP-4 inhibitor and metformin</i>
Empagliflozin, linagliptin, and metformin

Dapagliflozin, canagliflozin, and empagliflozin are SGLT2 inhibitors (SGLT2is) for treatment of type 2 diabetes mellitus (DM). Ipragliflozin, tofogliflozin, and luseogliflozin are approved in Japan. Sotagliflozin inhibits SGLT 1 and 2. SGLT2is preserve the estimated glomerular filtration rate (GFR) in diabetic, chronic kidney disease (CKD) and prevent cardiovascular disease³. They prevent the recurrence of heart failure even in nondiabetic patients⁴. However, they increase urinary tract and genital infections and can cause normoglycemic ketoacidosis in diabetics especially during infection or starvation⁵. Whereas SGLT2is and gliptins reduce hemoglobin type A1 fraction c (HbA1c) and major cardiovascular events similarly, SGLT2is fail to reduce stroke but have much greater beneficial effects in reducing heart failure and CKD events ⁶.

Anti-hyperglycemia Mechanism of SGLT2 inhibitors

The SGLT2 is expressed in the proximal tubule and mediates reabsorption of approximately 90 percent of the filtered glucose load. SGLT2 inhibitors promote the renal excretion of glucose and thereby modestly lower elevated blood glucose levels in patients with type 2 diabetes. The ability to lower blood glucose and glycated hemoglobin (A1C) levels is limited by the filtered load of glucose and the osmotic diuresis that is caused by this therapy¹.

SGLT2 is a low affinity, high-capacity luminal transporter in the S1 and S2 segments of the proximal tubule (PT) that normally reabsorbs about 97% of filtered glucose whereas SGLT1 is a high affinity, low-capacity transporter in the S3 segment that normally reabsorbs the remainder. SGLT1 is expressed also in the jejunum, thick ascending limb of the loop of Henle, macula densa (MD), and myocardial capillaries. The expression of SGLTs is increased in diabetes mellitus. The NHE3 (sodium:hydrogen exchange 3) increases the expression of SGLT2 and thereby links it to Ang (angiotensin) II, acidosis, oxidative stress, CKD, congestive heart failure (CHF), the sympathetic nervous system (SNS), adiponectin, and high-salt intake. Period and CLOCK gene can transcribe both NHE3 and SGLT1(Figure 1)⁷.

Moreover, although the currently developed SGLT2 inhibitors almost completely block proximal tubular glucose reabsorption, the measured inhibition is less than 50 percent based on urine glucose excretion⁸.

SGLT2 inhibitors only lower plasma glucose levels by blocking reabsorption of filtered glucose, which falls as plasma levels fall. Thus, they do not usually cause hypoglycemia in the absence of therapies that otherwise cause hypoglycemia.

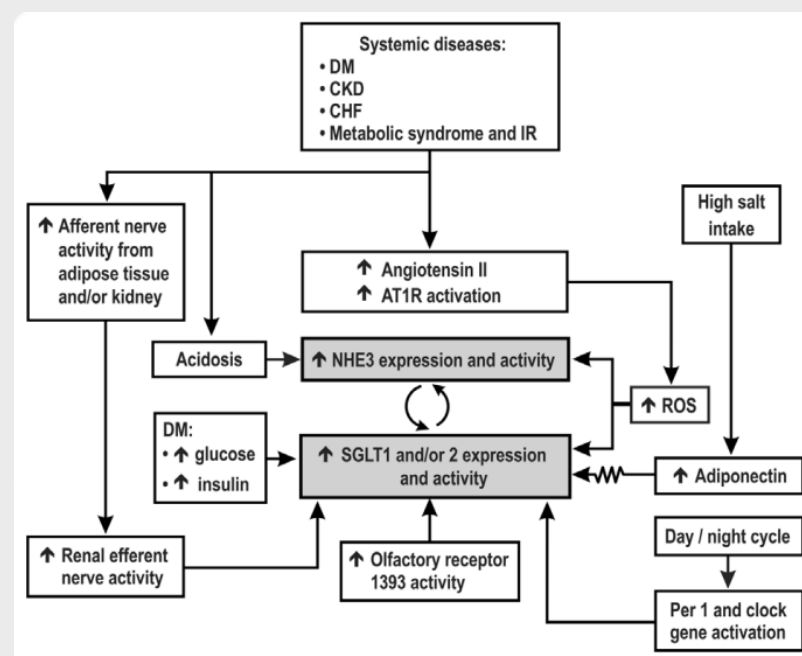


Figure 1. Diagram of expression and activity of SGLT (sodium-glucose linked transporters) 1 and 2 and NHE (sodium hydrogen exchanger 3). Ang II indicates angiotensin II; AT1R, angiotensin type 1 receptor; CHF, congestive heart failure; CKD, chronic kidney disease; DM, diabetes mellitus; IR, insulin resistance; Per 1, period 1 gene; ROS, reactive oxygen species; and SNS, sympathetic nervous system.

Indications of SGLT2 inhibitors

SGLT2 inhibitors are not considered as initial therapy for most patients with type 2 diabetes. Initial therapy with type 2 diabetes should begin with diet, body weight reduction, exercise, and metformin (in the absence of contraindications). In patients with cardiovascular or kidney disease, many SGLT2 inhibitors have demonstrated benefits for cardiovascular and kidney outcomes. However, SGLT2 inhibitors confer only modest improvement in glycemia and are costly, and long-term safety data on the effects of prolonged glucosuria are lacking.

SGLT2 inhibitors have therapeutic utility in the following settings:

1) In patients with overt atherosclerotic cardiovascular disease (CVD) not reaching glycemic goals with metformin and lifestyle modifications (empagliflozin, canagliflozin, and dapagliflozin, but not ertugliflozin)⁹.

2) In patients with heart failure not reaching glycemic goals with metformin and lifestyle modifications (empagliflozin, canagliflozin, dapagliflozin, and ertugliflozin).

3) To reduce decline in estimated glomerular filtration rate (eGFR) in patients with $eGFR < 90 \text{ ml/min/1.73m}^2$ (canagliflozin, dapagliflozin, empagliflozin, ertugliflozin). An initial short-term decrease in eGFR (of up to 30 percent) may be seen after starting SGLT2 inhibitor therapy, presumably due to a reduction in glomerular pressure. Following this initial decline, eGFR stabilizes. Greater initial reductions in eGFR warrant discontinuation of SGLT2 inhibitor therapy and evaluation for causes of acute kidney injury¹⁰.

4) As a third-line agent in patients not meeting glycemic goals on two oral agents (e.g., metformin and sulfonylurea) if for some reason combination metformin and insulin is not a therapeutic option.

5) As a third-line agent in patients not meeting glycemic goals on metformin and insulin therapy, in whom glucagon-like peptide 1 (GLP-1) receptor agonists are contraindicated and increasing insulin dosing would lead to weight gain¹¹.

6) As a second agent in patients with inadequate glycemic control on metformin who are unwilling or unable to consider injection therapy and in whom weight gain or risk of hypoglycemia is a significant issue.

Contraindications and precautions OF SGLT2 inhibitors

SGLT2 inhibitors should not be used specifically for the **treatment of hyperglycemia** in patients with:

- 1) Type 1 diabetes
- 2) Type 2 diabetes and $eGFR < 45 \text{ ml/min/1.73 m}^2$ (ertugliflozin), or $< 30 \text{ ml/min/1.73m}^2$ (empagliflozin, canagliflozin, dapagliflozin, bexagliflozin)
- 3) Prior diabetic ketoacidosis (DKA)

SGLT2 inhibitors have less glycemic benefit in patients with more severe kidney disease at initiation, and for the treatment of hyperglycemia. However, in patients taking insulin or insulin secretagogues, SGLT2 inhibitors can increase the risk of hypoglycemia.

SGLT2 inhibitors have been associated with the following conditions:

1) **Infection:** Genitourinary tract bacterial and yeast infections. In clinical trials, SGLT2 inhibitors conferred an approximate two- to four fold increased incidence of vulvovaginal candidiasis, reported in up to 10 to 15 percent of women. Similarly, in meta-analyses of trials, SGLT2 inhibitor use also led to a higher rate of vulvovaginal candidal infections (eg, 9.5 versus 2.6 percent in the control groups). SGLT2 inhibitors increase the rate of urinary tract infections (8.8 versus 6.1 percent) . In addition, the US Food and Drug Administration (FDA) has received reports of potentially fatal:

- Urosepsis and pyelonephritis¹²
- Necrotizing fasciitis of the perineum (Fournier's gangrene) ¹³

2) **Bone loss and fracture:** SGLT2 inhibitors should be used with caution in those at risk for falls and fracture. A possible mechanism, particularly for fractures occurring in older individuals after only 12 weeks of therapy, is **orthostatic hypotension** resulting in postural dizziness and falls. SGLT2 inhibitors may also adversely affect bone density through an **increase in tubular phosphate reabsorption** leading to fibroblast growth factor (FGF23) secretion and subsequent reduction in vitamin D activation¹⁴.

3) **Mild volume loss and hypotension:** Patients should be aware of possible side effects due to volume loss (eg, lightheadedness, dizziness, nausea). Blood pressure and kidney function should be monitored. **SGLT2 inhibitors should be withheld during times of volume loss or hypoperfusion (diarrhea, sepsis)** and restarted only once the patient has recovered. In older patients or in patients taking diuretics, angiotensin-converting enzyme (ACE) inhibitors, or angiotensin receptor blockers (ARBs), SGLT2 inhibitors may cause symptomatic hypotension. Patients

should be queried about orthostatic symptoms and instructed to monitor blood pressure, when feasible, during SGLT2 inhibitor initiation. Medications for hypertension might require proactive dose adjustment to reduce risk of hypotension.

4) **Lower extremity infection and amputation:** They should be used with caution in patients with risk factors for foot ulceration (e.g., neuropathy, foot deformity, vascular disease, and/or history of previous foot ulceration). Patients should be instructed to perform daily foot examination and should undergo routine examinations by their provider.

5) **DKA:** SGLT2 inhibitors increase risk of DKA. In several studies, "euglycemic" (usually meaning plasma glucose <250 mg/dL) DKA has been reported in patients with type 2 diabetes. In these individuals, **the absence of substantial hyperglycemia delays recognition of the problem by both the patients and the clinicians.** Serum ketones should be obtained in any patient with nausea, vomiting, or malaise while taking SGLT2 inhibitors. SGLT2 inhibitors should be withheld during times of increased DKA risk (e.g., infection, hospitalization, or surgery) and restarted only once the patient has recovered. The benefits and risks of therapy should be carefully assessed in individuals with factors predisposing to DKA (e.g., ketosis-prone type 2 diabetes, pancreatic insufficiency, drug or alcohol abuse disorder, ketogenic diets), and SGLT2 inhibitors should be avoided in individuals with a history of DKA unless a clear, modifiable risk factor for DKA (e.g., ketogenic diet, excessive alcohol use) has been identified and eliminated¹⁵.

In a network meta-analysis of 36 trials that evaluated drug therapies for type 2 diabetes, an increased risk of DKA was found only for SGLT2 inhibitors (OR 2.07, 95% CI 1.44-2.98, versus other therapies) . Similarly, in a population-based cohort study from Canada and the United Kingdom (more than 350,000 patients and 500 DKA events), SGLT2 inhibitors (empagliflozin, dapagliflozin, canagliflozin) compared with dipeptidyl peptidase 4 (DPP-4) inhibitors were associated with an increased risk of DKA (incidence 2.03 versus 0.75 per 1000 person-years, respectively, [HR 2.85, 95% CI 1.99-4.08]) . Among the three SGLT2 inhibitors, canagliflozin was associated

with the highest risk (HR 3.58 compared with 1.86 and 2.52 for dapagliflozin and empagliflozin, respectively)¹⁶.

6) **Acute kidney injury:** Since SGLT2 inhibitors can cause a mild degree of dehydration, they should be used with caution in conjunction with other medications that predispose to acute kidney injury (nonsteroidal anti-inflammatory drugs [NSAIDs], angiotensin-converting enzyme [ACE] inhibitors/angiotensin II receptor blockers [ARBs], diuretics) and comorbidities that might predispose to acute kidney injury (hypovolemia, heart failure, liver injury).

7) **Bladder cancer:** In clinical trials, 10 cases of bladder cancer were diagnosed among dapagliflozin users, five of which occurred in the first six months of dapagliflozin, a much shorter time interval than would be expected if dapagliflozin promoted tumorigenesis. However, these findings have prompted the FDA to recommend post marketing surveillance studies. There is no long-term safety data regarding the effects of chronic glucosuria on the urinary tract.

Antihypertensive actions of SGLT2 inhibitors

Empagliflozin reduces daytime and nighttime systolic blood pressure (BP) even in patients with CKD stage 3b despite little reduction in HbA1C. These findings dissociate antihypertensive from antihyperglycemic effects¹⁷.

SGLT2is cause a modest **diuresis** in euglycemic subjects that is enhanced by hyperglycemia and persists in CKD stage 3 to 4, despite causing little glycosuria prompting studies on nephron Na⁺ handling beyond osmotic diuresis. Indeed, SGLT2is reduce PT fluid reabsorption by 27%. Most Na⁺ are reabsorbed in the PT in exchange for H⁺ by NHE3 whose activity is increased by luminal glucose. Packer has proposed that the activation of NHEs mediates diabetic complications¹⁸. Although cardiomyocytes do not express SGLT2, SGLT2is inhibit cardiac Na⁺: H⁺ exchange perhaps because they block NHEs directly by an off-target action. However, SGLT2 and NHE3 also are interlinked by membrane associate protein that interacts via post synaptic density protein/tight junction protein 1 (PDZK1). Thus,

SGLT2 increases the activity of NHE3 as well as the sodium-phosphate exchanger type IIa, the organic cation transporter, the chloride-formate exchanger, the urate-anion exchanger, and the cystic fibrosis transmembrane regulator of Cl⁻ transport (Figure 2A)⁷.

These widespread effects on the PT may explain why SGLT2is reduce BP in CKD stage 3 or 4 despite little glycosuria. SGLT2is inhibit NHE3 and reduce HCO₃⁻ absorption in the PT in the absence of luminal glucose. This should cause metabolic acidosis. However, genetic deletion of NHE3 creates only modest acidosis because of increased ammonia genesis. Indeed, SGLT2is increase ammonia excretion 4-fold perhaps, because PT acidosis reduces intracellular [K⁺] that stimulates ammonia genesis¹⁹. Thus, SGLT2 is a component of an interactive PT resorptive platform whose blockade impairs Na⁺ reabsorption rather profoundly even in the absence of luminal glucose. SGLT2is increase the glucose and osmolality of tubular fluid sufficient to hinder H₂O reabsorption and reduce tubular fluid: plasma [Na⁺] that may induce paracellular Na⁺ secretion by the S3 segment of the PT⁴¹ (Figure 2B). A decreased PT reabsorption of Na⁺ with SGLT2is increases the renal outer cortical PO₂, whereas an increased loop of Henle reabsorption of Na⁺ decreases the medullary PO₂.

Body Weight and Obesity

SGLT2is reduce body weight by about 1 to 3 kg¹² by loss of fat (50%–75%), body water (15%–35%), and protein and minerals (10%)¹⁷. Glycosuria causes a negative calorie balance although this is offset by hyperphagia. SGLT2is switch some glucose metabolism to fatty acids and ketones and increase the glucagon/insulin ratio and fat utilization. Almost 40% of the antihypertensive action of canagliflozin might be attributed to weight loss. SGLT2is reduce plasma volume (PV) and body weight by 1 to 2 weeks, but the early fall in PV is restored by 12 weeks, yet the hematocrit remains elevated. This indicates that the blood volume (BV) is increased, yet the BP remains reduced²⁰.

In another study, the early reduction in PV with dapagliflozin was matched by an increase in red cell mass (RCM) with unchanged BV. SGLT2is increase plasma erythropoietin transiently and reduce the extracellular fluid volume and intracellular fluid volume and total body water. Thus, the early reduction in PV with SGLT2is is offset by a rise in RCM that maintains, and may eventually even increase the BV, but there is a persistent reduction in extracellular fluid volume, intracellular fluid volume, total body water, and BP. The PV is restored by 3 months, yet the hematocrit remains elevated suggesting a selective reduction in extra-and intracellular water. Although the early reduction in PV with SGLT2is has been ascribed to the diuresis, diuretics do not increase RCM, erythropoietin, or hematocrit. Thus, changes in body fluids after SGLT2is are not characteristic of classical diuretics. An alternative explanation is that the changes in body fluids are in response to erythropoietin release by renal medullary hypoxia.

A reduction in PV without a reduction in BV is unlikely to reduce the BP or to provide cardiovascular disease protection. Indeed, the failure of SGLT2is to reduce stroke, despite a fall in BP and cardiovascular disease, could be a consequence of a persistent increase in hematocrit since this increases the risk for stroke, hypertension, CKD, and fluid retention.

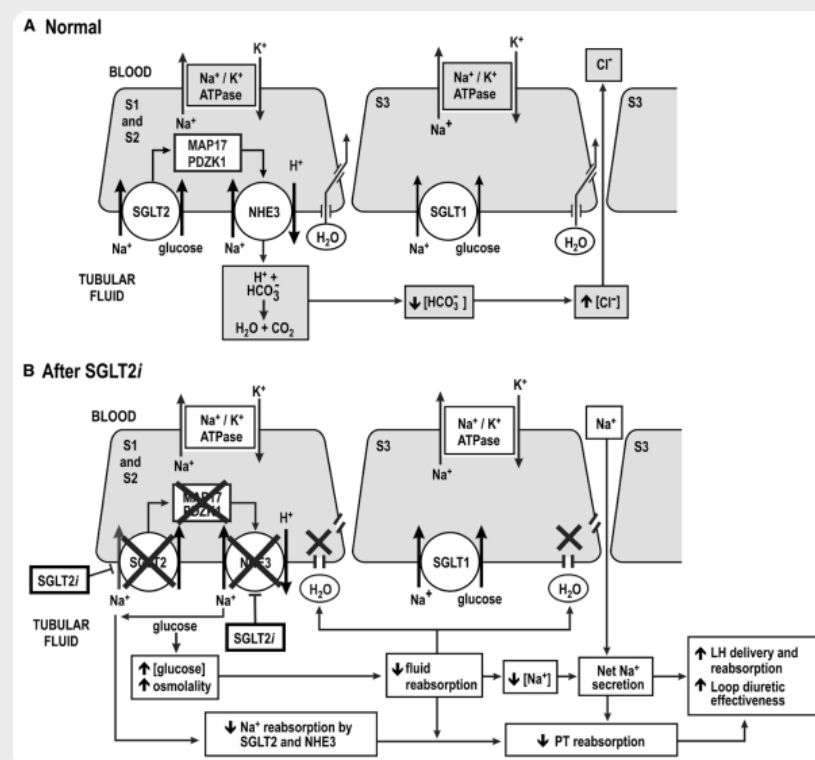


Figure 2. Depiction of SGLT2 (sodium-glucose linked transporter type 2) in the normal regulation of proximal tubule (PT) reabsorption and the effects of SGLT2 inhibition. SGLT2

normally is linked to the NHE3 (sodium hydrogen exchange 3) by MAP17 and PDZK1 thereby enhancing Na^+/H^+ exchange, increasing the tubular fluid $[\text{Cl}^-]$ sufficiently to lead to its passive paracellular reabsorption. After SGLT2 inhibition (B), increased tubular fluid glucose and osmolality impairs water reabsorption that dilutes the tubular fluid $[\text{Na}^+]$ to induce paracellular secretion of Na^+ . The enhanced delivery of NaCl to the loop of Henle enhances the effectiveness of loop diuretics. LH indicates loop of Henle; MAP17, membrane associated protein 17; and PDZK1, post synaptic density protein 95/tight junction protein 1.

Heart failure benefits

Loop diuretic natriuresis is increased by 36% after 1 week of dapagliflozin likely because of enhanced delivery of NaCl to the loop of Henle, ²¹thereby enlarging the target for loop diuretics (Figure 3A). Dapagliflozin natriuresis is increased 3-fold after 1 week of bumetanide likely because Ang II generated by loop diuretic actions, activates SGLT2, thereby enhancing the target for the SGLT2is (Figure 3B). Thiazides and SGLT2is also are synergistic. These effects may prove beneficial in heart failure. SGLT2i and an ARB (angiotensin blocker) provide additive renal protection in a rat model, while SGLT2is reduce albuminuria in patients with type 2 diabetes mellitus receiving ACE (angiotensin-converting enzyme) inhibitors or ARBs. Thus, SGLT2is are at least partially additive with renin system inhibitors.

Luminal glucose competes with uric acid for reabsorption via the PT URAT-1 (urate transporter 1). SGLT2is increases luminal glucose and may inhibit URAT-1 directly thereby increasing renal clearance of uric acid substantially²². Since uric acid induces reactive oxygen species (ROS), inflammation, vascular proliferation, and renal damage, reduced plasma urate by SGLT2is may maintain vascular and renal structure and function. Moreover, SGLT2is reduce vascular and renal ROS, inflammation and renal fibrosis and improve endothelial NO and function and aortic stiffness. All of these could reduce BP. SGLT2is can vasodilate isolated blood vessels directly and increase vascular nitric oxide perhaps secondary to blockade of

NHE1. These endothelial effects of SGLT2is likely contribute to organ protection.

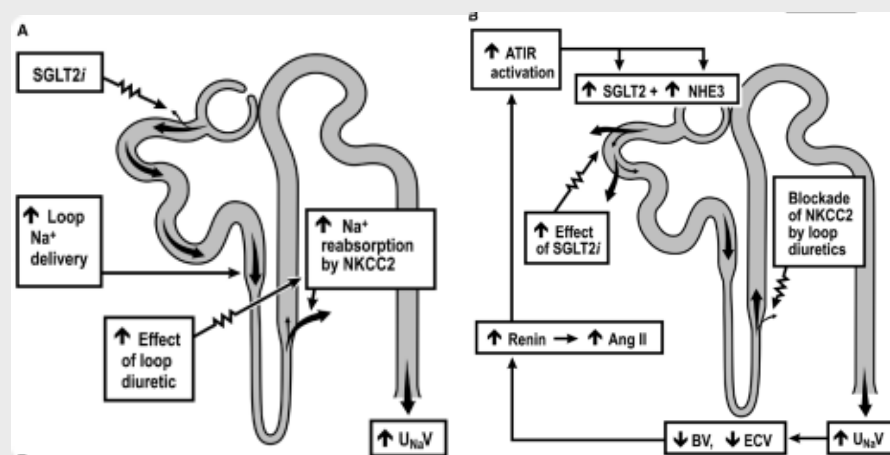


Figure 3. Synergistic natriuretic interactions between a sodium-glucose linked transporter type 2 inhibitor (SGLT2i) and a loop diuretic. Inhibition of proximal tubule reabsorption by SGLT2i increases delivery to the $\text{Na}^+/\text{K}^+/\text{2Cl}^-$ (NKCC2) cotransporter and hence loop diuretic effectiveness (A). Loop diuretics increases renin release and Ang (angiotensin) II generation that accentuates the AT1R (angiotensin type 1 receptor) to increase the expression of SGLT2 and NHE3 (sodium hydrogen exchanger type 3) and hence increase the natriuresis with SGLT2is (B). BV indicates blood volume; and ECV, extracellular fluid volume; and U_{NaV} , urinary sodium excretion.

In summary, many factors contribute to the beneficial effects of SGLT2is on BP and to their protection of the kidney and cardiovascular systems (Figure 4).

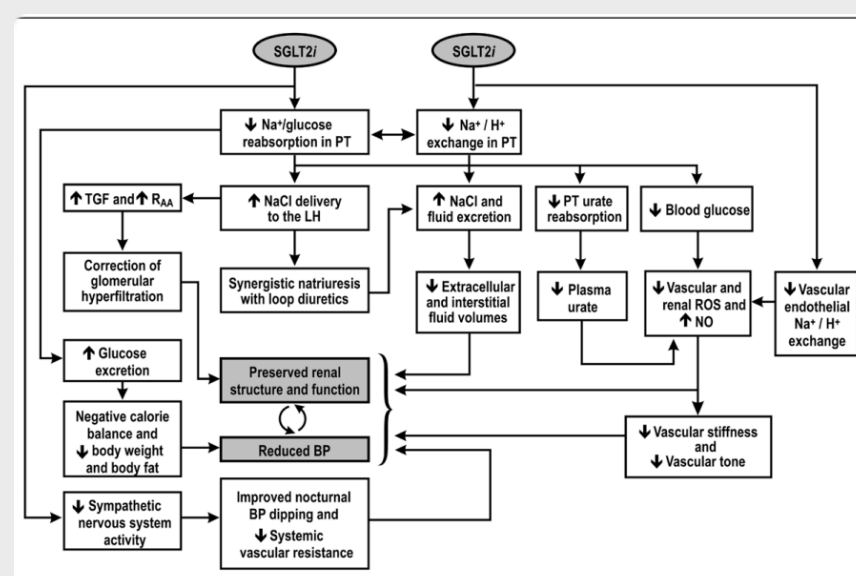


Figure 4. SGLT2 (Sodium-glucose linked transporter type 2) inhibitors preserve kidney function and reduce blood pressure (BP) in patients with diabetes mellitus. LH indicates loop of Henle; PT, proximal tubule; RAA, resistance in the renal afferent

arteriole; ROS, reactive oxygen species; SNS, sympathetic nervous system; and TGF, tubuloglomerular feedback.

Perioperative anesthesia management for patients on SGLT-2is

According to last year published 2024 AHA/ACC/ACS/ASNC/HRS/SCA/ SCCT/SCMR/SVM Guideline for Perioperative Cardiovascular Management for Noncardiac Surgery²³, “SGLT2i, noninsulin glucose-lowering agents that facilitate glycemic control by inhibiting renal glucose reabsorption and thus promoting glycosuria, must be **discontinued 3 to 4 days before surgery**. A rare complication of these agents is euglycemic diabetic ketoacidosis.” An alternative plan for glycemic management should be implemented until the elevated risk of acute kidney injury, organ hypoperfusion, and acidosis subsides²⁴.

At the beginning of 2025, Medstar Health Medical Anesthesia Group(MMGA) implemented SGLT-2i guideline as following:

Requirements and Guidelines for Implementing the Policy

1. Preoperative Management

a. SGLT2i medication should be held prior to DOS, whether given alone or as part of a combination medication

Hold ertugliflozin for four (4) days prior to DOS

ii. Hold canagliflozin, bexagliflozin, empagliflozin, dapagliflozin for three (3) days prior to DOS

2. Day Of Surgery Management

a. For Patients who did hold their SGLT-2i as recommended, proceed to surgery following MMGA Glucose management guidelines.

b. For Patients who did not hold their SGLT-2i as recommended, the goal is to manage **the risk of euglycemic diabetic ketoacidosis (eDKA) , rather than cancel the procedure.**

Resuming a postoperative diet is key to decision making.

c. Patients who will not be NPO postoperatively (Outpatients, Same Day Admit Patients, Inpatients)

1. Non-diabetic patients

No intervention – proceed with the procedure

2. Diabetic patients

a. Send stat **BMP** (basic metabolic profile) and **Beta-Hydroxybutyrate level (BOHB)** pre-op

b. Proceed with planned procedure, if otherwise appropriate, while labs are pending

- GI upset, nausea, vomiting may be signs of eDKA and the decision to proceed should be delayed pending labs results

c. If anion gap ≤ 12 , no further intervention is needed. Postop disposition as planned

d. If anion gap > 12 and BOHB > 2, this represents eDKA.

i. Initiate infusions of D5W at 125 ml/hr and regular insulin at 0.05 units/kg/hour.

ii. Check glucose level q60 minutes and adjust insulin infusion as needed to maintain glucose 140-180 mg/dl.

iii. Do not adjust D5W infusion.

iv. Notify surgical team to admit for management of eDKA.

v. We expect this to be a very infrequent event and should be reported through SafetyNet

e. If anion gap > 12 and BOHB < 2, this is not eDKA. Evaluate for other causes of anion gap acidosis and proceed if appropriate

f. If the patient cannot tolerate PO intake in PACU, repeat stat BMP two hours after PACU arrival and follow guideline for postop NPO patients below.

ii. Patients who will be NPO postoperatively (Same Day Admit Patients, Inpatients):

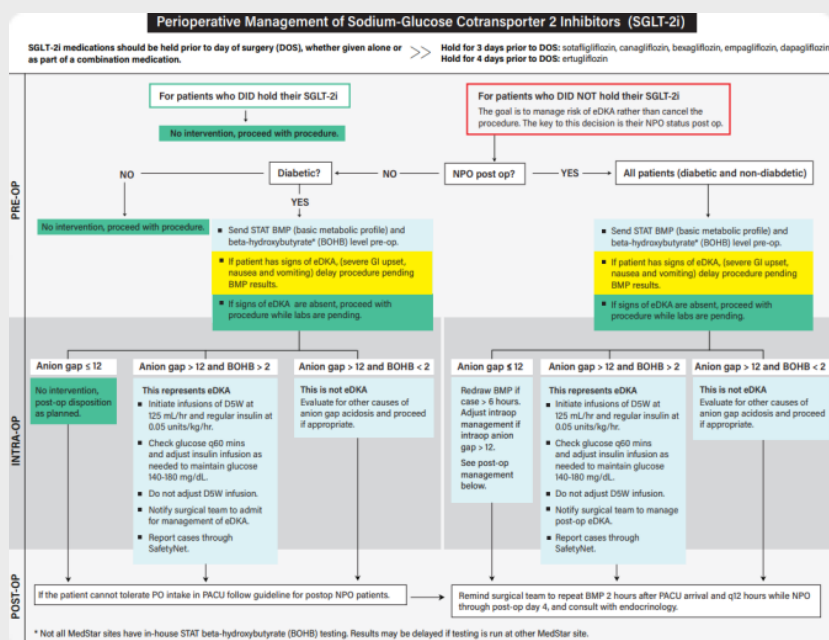
1. All Patients (Diabetic and Non-Diabetic)

- a. Send stat BMP (basic chemistry profile) and Beta-Hydroxybutyrate level (BOHB) pre-op
- b. Proceed with planned surgery, if otherwise appropriate, while labs are pending. However, **GI upset, nausea, vomiting may be signs of eDKA** and the decision to proceed should be delayed pending labs results
- c. If BMP anion gap ≤ 12 , redraw BMP if case > 6 hours. Adjust intraoperative management if later anion gap > 12 . See postop management below
- d. If anion gap > 12 and BOHB > 2 , this represents eDKA.
- i. Initiate infusions of D5W at 125 ml/hr. and regular insulin at 0.05 units/kg/hour.
- ii. Check glucose level q60 minutes and adjust insulin infusion as needed to maintain glucose 140-180 mg/dl.
- iii. Do not adjust D5W infusion.
- iv. Notify surgical team to manage postop eDKA.
- v. We expect this to be a very infrequent event and should be reported through SafetyNet
- e. If anion gap > 12 and BOHB < 2 , this is not eDKA. Evaluate for other causes of anion gap acidosis and proceed if appropriate
- f. Remind surgical team to repeat BMP 2 hours after PACU arrival and q12 hours while NPO through post-op day #4

Recently, we encountered some push back from our gastroenterologists and cardiologists while implementing the guidelines to our NORA sites, especially for outpatient procedures. GI Nurse Practitioners and physicians often confuse SGLT-2i with GLP-1A due to their common weight loss feature, so they ask their patients to hold SGLT-2i for one week instead of 3-4 days which leads to poorly controlled existing heart failure and pre-procedure hyperglycemia requiring insulin administration and potential exacerbated hypoglycemia response after administering insulin. Cardiologists at EP lab argue that SGLT-2is are being used for heart failure management which need to be continued to optimize their overall cardiac condition for their heart arrhythmia intervention. Even though holding SGLT-2i is justified for longer and bigger open-heart cases, it should not be a concern for outpatient short procedures since the incident of euglycemic ketoacidosis is extremely rare for their patients.

ASA Community Communication Column discussed this issue on May 15, 2025. People routinely work at endoscopy centers mentioned if patients arrive for a procedure and don't stop their -Flozins, they almost always do the case unless there is prolonged fasting /dehydration leading to symptomatic eDKA presentation. For EGD, certainly will proceed with the procedure without extra testing if patient ate dinner the night before and will resume food shortly afterwards, there is no risk of eDKA. For colonoscopy, there is slightly higher risk of eDKA, for those patients who fail to stop their SGLT-2is, it's better to have some Carb Drink the night before and have their procedure done in the morning instead of late afternoon.

I personally agree with their opinions that the risk of eDKA for outpatient procedures is very low, hence the yield of BMP and BOHB is extremely low. Given the time consuming and low yield to do the blood test for patients on SGLT-2i but failed to stop 3-4 days prior to the ambulatory procedure, I usually omit the test for eDKA unless clinically indicated. For some inpatients with prolonged NPO due to GI bleeding or dysphasia, their SGLT-2is usually have been held already since admission, if not, we'll request the BMP and Beta-Hydroxybutyrate before the procedure.



So far, no official SGLT-2i guideline from Society of Ambulatory Anesthesiologists has been published, we are still waiting for our Medstar Diabetic Council for their professional input on this issue.

Another problem is pre-procedural anesthesia assessment. In contrast to surgical patients who often are interviewed by phone or show up in person to pre-anesthesia assessment clinic (PAC) prior to surgery, over PAC they often receive detailed instruction on holding their medications, our NORA patients do not go through PAC system. Our proceduralists usually don't ask their outpatients to stop taking SGLT-2i 3-4 days before their procedures or give their patients wrong instruction on holding SGLT-2is. With majority of outpatients on SGLT-2i are completely asymptomatic pre-procedures and are capable of resuming PO intake in the PACU shortly after their EGD, colonoscopy, cardioversion, EP study +/- ablation, pacemaker, ICD and IR out-patients procedures etc., most of anesthesiologists work at NORA sites choose not to follow perioperative SGLT-2i guideline to get preop lab test or infuse D5 during the procedure. As far as I know, a few of our patients did get blood BMP and Beta-Hydroxybutyrate level, none of them had positive results indicating eDKA.

In a recently published JAMA Surgery retrospective matched case-control study, patients treated with SGLT2i had a slightly but statistically significantly higher risk of postoperative eDKA compared with control patients². In this cohort, an eDKA incidence of 29.6% among surgical patients using SGLT2i was identified, which is higher than the incidences previously reported as 22.6%, possibly because all of the studied patients were having emergency operations instead of elective surgeries as in the other clinical trials. It also showed a lower risk of AKI and 30-day mortality while on SGLT-2is. This paper was written by UCSF and Washington University anesthesiologists, they pointed out that the consequences of developing perioperative eDKA are not fully understood; however, perioperative eDKA may necessitate escalated interventions (i.e., insulin administration or continuous dextrose infusion), which could be associated with an increased risk of prolonged hospitalization or unplanned admission to an intensive care unit. The median

hospital length of stay among the patients presenting with eDKA increased by 3 days, 6 days for those with eDKA vs 3 days for those without eDKA.

Is this study presenting a hint that we have been over testing eDKA or is not necessary to test every single patient on SGLT-2i at least before ambulatory procedures? Clearly, we need to have more research to further clarify the issue. At least for outpatient procedures, we have more wiggle room deviating from our SGLT-2i guideline.

I would like to hear any feedback from other CASA members in terms of SGLT-2is management for ambulatory surgeries.

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(王清摄影作品, Sunset at Saguaro National Park, Arizona)

Original Article (原创文章)**Nitric Oxide and Cardiovascular Health: Role of the Endothelium and Emerging Nitric Oxide Protectants**

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Abstract:

Nitric oxide (NO) plays a pivotal role in maintaining cardiovascular health by regulating vascular tone, inhibiting platelet aggregation, and modulating endothelial function. As a key endothelium-derived relaxing factor, NO supports vasodilation and prevents atherogenesis. Impaired NO bioavailability is a hallmark of endothelial dysfunction and a major contributor to hypertension, atherosclerosis, and other cardiovascular diseases. One of the recent research focuses has been on the development of NO protectants, which may preserve or restore endothelial NO signaling. Thus, NO protectants may serve as promising new therapeutic strategies. This review will discuss the biosynthesis and physiological roles of NO, its relationship with endothelial health, and the current landscape of NO protectants aimed at mitigating cardiovascular risk.

Keywords: Nitric oxide, cardiovascular health, endothelium, nitric oxide protectants, endothelial dysfunction, NO donors, eNOS, vascular biology

I. Introduction

Cardiovascular disease (CVD) remains a leading cause of morbidity and mortality globally, with 20.5 million deaths recorded in 2021 [1]. An important component in the pathophysiology of CVD is endothelial dysfunction, which is often characterized by reduced nitric oxide (NO) bioavailability [2,3]. Nitric oxide, a gaseous signaling molecule synthesized by endothelial nitric oxide synthase (eNOS), is essential for vascular homeostasis [2,3]. Thus, NO preservation by NO protectant(s) may potentially be beneficial in maintaining cardiovascular health [4]. This manuscript explores the physiological significance of NO in cardiovascular health, its regulation by the endothelium, and the potential of nitric oxide protectants as therapeutic interventions.

II. Nitric Oxide: Synthesis and Mechanisms of Action

NO is produced endogenously from L-arginine by nitric oxide synthase (NOS), of which endothelial NOS (eNOS) is the key isoform in endothelial cells. The production of NO is calcium/calmodulin-dependent and tightly regulated by shear stress, oxidative stress, and various biochemical signals. Upon synthesis, NO diffuses into vascular smooth muscle cells and activates soluble guanylate cyclase (sGC), leading to increased cyclic GMP (cGMP) levels and subsequently inducing vasodilation and reduction in vascular tone [5, Figure 1]. Additionally, NO exerts anti-inflammatory, antithrombotic, and antiproliferative effects, making it a critical mediator of vascular health [2,3].

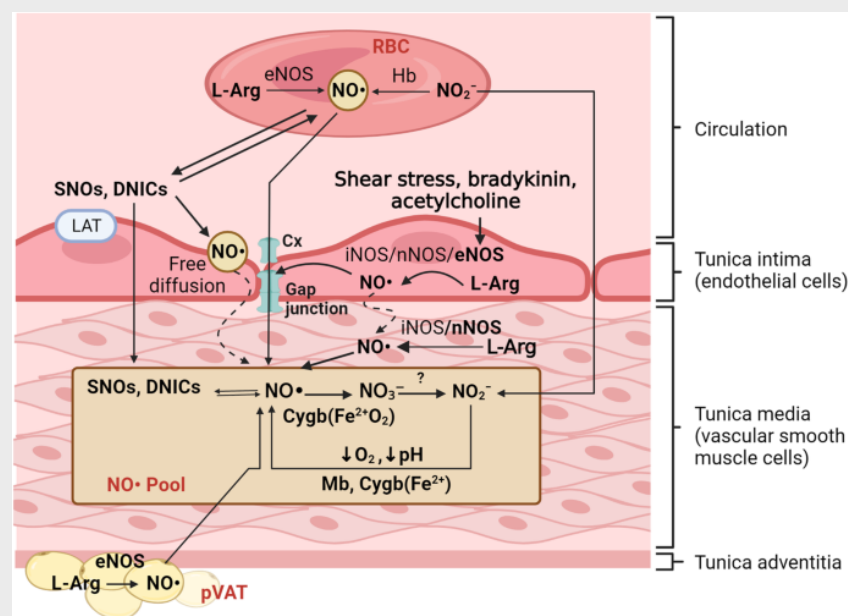


Figure 1 Nitric oxide syntheses and effects on vascular smooth muscle cells [5]

III. Role of the Endothelium in NO Regulation

The endothelium is not only a barrier between blood and vascular wall and tissue but also an active endocrine organ [6]. Endothelial cells regulate vascular tone through the release of vasoactive substances, with NO being paramount. Healthy endothelium ensures optimal NO production, facilitating the following effects.

Relaxation of vascular smooth muscle: NO relaxes vascular smooth muscle by increasing the concentration of cyclic GMP (cGMP) within the muscle cells. This increase in cGMP activates myosin light chain phosphatase (MLCP), which dephosphorylates myosin light chains, leading to smooth muscle relaxation. NO also reduces intracellular calcium concentrations, which further contributes to relaxation [3].

Inhibition of leukocyte adhesion: NO inhibits leukocyte adhesion to endothelial cells, a process essential for the immune system's response to inflammation and infection. NO's anti-adhesive effects are mediated by its regulation of adhesion molecules on both leukocytes and endothelial cells, as well as by its ability to reduce superoxide radical formation [7].

Suppression of vascular inflammation: NO suppresses vascular inflammation by regulating vascular tone, inhibiting platelet

activity, and preventing leukocyte adhesion to the endothelium. It can also influence the proliferation and apoptosis of vascular cells, alter cellular respiration, and impact the intracellular redox environment. Furthermore, nitric oxide can reduce the expression of adhesion molecules, leading to a decrease in inflammatory cell recruitment into the vessel wall [8].

Prevention of thrombosis: NO plays a crucial role in preventing thrombosis by inhibiting platelet activation and adhesion to the endothelium, thus preventing thrombus formation. It also dilates blood vessels, contributing to maintaining healthy blood flow and preventing blood clots [9].

Endothelial dysfunction results in diminished NO output and is often an early indicator of CVD. Contributing factors may include oxidative stress, hyperglycemia, dyslipidemia, smoking, and aging[10].

IV. Nitric Oxide and Cardiovascular Diseases

Numerous studies have shown that impaired NO signaling is linked to the pathogenesis of multiple medical conditions.

Hypertension: NO plays a crucial role in maintaining healthy vascular function, and its deficiency leads to impaired endothelium-dependent vasodilation, promoting vasoconstriction and increasing overall resistance [11].

Atherosclerosis: Low NO levels promote endothelial activation and plaque formation. NO is a crucial molecule for maintaining endothelial health and preventing plaque development. When NO levels are low, it can lead to endothelial dysfunction, which is a key factor in the development of atherosclerosis [12].

Heart failure: a disruption in the NO-cGMP signaling pathway is a key contributor to myocardial remodeling and dysfunction. This pathway, involving nitric oxide (NO), guanylate cyclase (GC), and cyclic GMP (cGMP), normally plays a crucial role in regulating vascular tone and cardiac function. When this signaling is impaired, it leads to structural and functional changes in the heart, ultimately contributing to heart

failure. Diabetes-related vascular disease: Hyperglycemia impairs eNOS activity and NO bioavailability [13].

Based on the above-mentioned discuss, therapeutic approaches that aim to restore NO signaling could mitigate these pathologies.

V. Nitric Oxide Protectants: Emerging Therapeutic strategies

Given the importance of NO in maintaining vascular health, NO protectants have garnered enormous interest. These agents aim to enhance NO availability, prevent its degradation, or mimic its effects. Currently there are several categories of NO protectants. Antioxidants (e.g., Vitamin C, polyphenols): Antioxidants neutralize free radicals, which can degrade NO. Foods rich in antioxidants, like fruits, vegetables, nuts, and seeds, can help maintain stable NO levels.

eNOS cofactors: eNOS requires several cofactors to function properly. These include tetrahydrobiopterin, flavin adenine dinucleotide, flavin mononucleotide, heme, calcium/calmodulin, and NADPH. Tetrahydrobiopterin is particularly crucial for optimal eNOS activity and prevents the enzyme from uncoupling and producing superoxide instead of nitric oxide.

Nitrate and nitrite supplementation: Leafy greens like spinach, arugula, cabbage, and kale are good sources of nitrates, which the body converts into NO. Regularly consuming these foods can help sustain adequate NO levels.

Dietary supplements: L-citrulline and L-arginine are two common supplements that can increase NO bioavailability. Beetroot juice, a rich source of nitrates, is another supplement that can boost NO levels.

Phosphodiesterase-5 inhibitors (e.g., sildenafil): prolong NO signaling by inhibiting the breakdown of cGMP, a second messenger that is crucial for smooth muscle relaxation and

vasodilation. This inhibition leads to increased cGMP levels, which in turn promotes vasodilation and improved blood flow.

sGC stimulators/activators are two classes of agents that increase the activity of soluble guanylate cyclase (sGC), an enzyme involved in the NO-sGC-cGMP pathway. They play a crucial role in regulating blood vessel function and are being explored for various cardiovascular and pulmonary conditions.

Novel compounds and natural products are also under investigation for their potential to act as NO donors or enhancers in the cardiovascular system [14].

VI. Challenges and Future Perspectives

Despite promising preclinical results, translating NO protectant-based therapies into clinical practice has been challenging. There are some key issues to be solved. Targeted delivery and sustained NO release will be needed since NO is very short-acting, typically ranging from 0.1 to 5 seconds. Thus, the concentration of NO in the body can rapidly decreases over time if no continued release of NO into blood circulation or to a specific area in the body tissue/organ. Using special vehicle to deliver NO to a specific region can be difficult and troublesome [15]. If NO is administered systemically, it may cause significant hypotension due to its potent vasodilative effects. Management of hemodynamic stability will need to be addressed [16]. And metabolism of NO has significant individual variations. This can be influenced by factors like genetic background, age, sex, health status, and gut microbiota composition, impacting the individual's response to NO-related effects. Understanding these differences is crucial for personalized medicine and designing effective treatments.

Emerging technologies such as nanoparticle-based NO delivery, gene therapy to enhance eNOS expression, and personalized medicine approaches could hopefully help overcoming these barriers and offer feasible therapeutic clinical options [14].

VII. Summary

NO is a fundamental regulator of endothelial and cardiovascular function. The decline in NO bioavailability is a key driver of cardiovascular diseases. Therapeutic strategies aimed at preserving or enhancing NO signaling—through the use of NO protectants or NO donors— may offer significant promise for preventing and treating cardiovascular diseases and other pathological conditions as diabetes mellitus. Continued research is warranted to optimize these approaches and translate them into effective clinical interventions.

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王海明医生回忆录（续 9）

17. CASA的创建 《留学生之歌》唱响

2002 年 12 月 7 日，纽约麻醉年会上，我非常幸运地巧遇另九位美籍华人麻醉医师（中国大陆医学院毕业，又入美国麻醉领域）。



王海明 (10/1/1959 -08/23/2019) 1983年毕业于北京医学院，1985年赴美。1994年从Boston Elizabeth and MGH完成麻醉科培训。于2002年创立CASA 并出任首任会长，也曾任CASA Bulletin责任编辑。为CASA和中美麻醉医学的交流作出了杰出贡献。

一起去附近中餐馆（至尊宝）午饭，我提议组创美国华人麻醉医学会（Chinese American Society of Anesthesiology, CASA），大家一致赞同。当即分工，我被众人推选为首任会长。我回家当晚，起草《创会宣言》，热血沸腾，挥笔疾书，《留学生之歌》首稿就这样诞生了！周末，带着歌词，我顶风冒雪去波士顿齐雅明和沙金华家，请音乐指挥齐雅格博士谱

了曲，请男高音胡冰试唱。从下午反复推敲至次日凌晨。我们均很自豪。因为，我们之前从未闻有《留学生之歌》！2003 年 1 月 1 日，中国新华社发稿“《留学生之歌》唱响美国纽约！”歌词和简谱刊于《光明日报》和《光明网》，《世界日报》，巴黎的《欧洲时报》，《人民日报》海外版，《美国华人医师会（ACAP）月刊》……五线谱有降 B，G。十数年来，众多师生提了许多好建议，歌词越改越好。我认为这是全世界中国留学生、学者、华侨的歌！希望能唤起大家的共鸣！……青春之歌多么悠扬！

CASA 宗旨有二：1. 帮助会员们；2. 促进中美麻醉医学交流。

筹备小组有10人：

王海明：首任会长；

陈国纲：付会长；

李迺曦：秘书长；

王长征：秘书助理；

谢燎阳：司库；

黄希松：司库助理；

何小莉、彭敏中 均是主治医师；

唐越：住院医师代表；

陶青：住院医师。

上述十人中，王海明和李迺曦已通过麻醉专科执照。当时，就分工，王海明：负责联络全美麻醉界华人和中国大陆、台湾、香港等地同仁；起草创会宣言。李迺曦：负责找律师注册学会；起草会章。王长征和谢燎阳等联系成立大会场地（选了：Sheraton, 法拉盛中心）。

2003 年2月9日，CASA 如期举行成立会议，50余人参加。王海明推荐周海峰医师为第二任会长，全体会员一致赞同。康奈尔医学院的 Fun Sun Yao MD 姚繁盛教授亲临会场，代表华人麻醉前辈致辞祝贺。《世界日报》、《星岛日报》等报道了CASA 成立！

CASA 网站www.chineseasa.org 由李迺曦、王海明、陈国纲、谢燎阳等负责设立。

CASA 会徽：王海明和女儿（王美玲）设计，2003。

CASA 会旗：王清、李鸥和王海明设计，2003年10月在旧金山制成。

很快，我将美国和加拿大著名麻醉教授们聘请为CASA荣誉会员。包括来自哈佛大学医学院：Letty Liu MD, Philip Liu MD；康奈尔医学院：Fun Sun Yao MD 姚繁盛，Jeffrey Yin Foh Ngeow MD 饶仁和，Spencer Liu；哥伦比亚大学医学院：Leila Pang

MD ; Lena Sun MD (孙心仪); 约翰霍普金斯大学医学院 : Thomas Toun (童瑞恭); 新泽西医学和牙科学院: Wen-shien Wu MD (吴闻咸); 宾夕法尼亚大学医学院: Albert Cheung MD, PhD; 芝加哥大学医学院: Chung - Yuan Lin 林重远; 犹他州立大学医学院: K C Wong (黄光中); 加州大学: Chingmuh Lee (李清木); 多伦多大学医学院: Frances F. Chung MD (钟芳亭); 加拿大西安大略医学院: Davy Cheng MD (郑仲煊); 多伦多: Vincent Chan MD (陈永旋); 爱荷华大学医学院: Cynthia Wong MD (王道真); 纽约州立大学石溪分校: Tong J Gan MD (颜东裕); 香港的 Tony Jin; 台湾的王志中; 大陆的谢荣, 罗爱伦, (李树人), 吴新民, 刘进, 黄宇光, 姚尚龙, 于布伟, 熊利泽, 马虹, 俞卫锋, 邓小明, 米卫东, 巢卫, 谢仲淙, 曾因明.....

学会成立后, 曾多次组织活动 (在爱因斯坦医学院, Citi-bank 聚会厅, 宾州Poconos 度假中心等), 帮助会员们备考麻醉专科笔试和口试。2005年起, 每年组团回中国讲学。每年在全美麻醉年会期间举办周六交流晚会。

CASA人才辈出! 不仅在美国大家互相帮助, 而且力促中国麻醉与世界接轨!

美国华人麻醉医学会(CASA)的月刊越办越好。初创学会时, 我经常向会员们发信, 报告学会的进展。那时, 女儿王美玲(高中)是我的秘书。常常是我思索后口述, 美玲帮我打字。发文速度很快! 后来, 美玲去了哈佛大学, 二女儿王美慧接班成为我的秘书。美慧去宾大后, 我曾试着自己写, 确实慢了许多。

唐越 (David Yue Tang MD)任会长时, 创办CASA每月通讯, 不久升级为靓丽的CASA月刊。那时, 胡宗元(原北医医学系78级 - 5班, 毕业后曾在中华医学会负责编辑, 来美国费城后又学计算机, 博学又热情)负责排版, 月刊页面精美, 贡献巨大。月刊曾发表了: 《Fun Sun Yao 姚繁盛教授简传》, 张晓燕医师的《简介恩师李清木教授》, 王海明专访《中国麻醉学先驱-谢荣教授》, 《李树人教授简传》, 刘立新教授介绍《Tong J Gan 颜东裕教授》, 台湾麻醉学会《王志中教授》, 武汉《姚尚龙教授》, 通过王雪华教授获稿《艾世勋教授回忆录》, 黄宇光教授著《罗爱伦教授行医50年》, 《金士翱教授》, 盛炜《见证神迹

传奇》, 《疼痛诊疗先驱饶仁和教授》, 陈晓云和王东信著《一代宗师: 谢荣教授传记》, 余大为前辈《美国临床麻醉四十年》, 王家双撰写《中国现代疼痛医学发展回眸》等。王家双文中盛赞的韩济生院士, 是我熟悉的北医生理学教授, 韩教授妻子在科学院工作, 儿子韩松平是我的学长(北医基础医学77级)、女儿是我大学同年同学韩一虹。韩济生教授送纪如荣(南京大学生物系, 中科院上海所博士, 韩济生教授的博士后)去瑞典凯若琳斯卡进修, 纪如荣后来去哈佛大学医学院, 现在杜克大学任神经科学和麻醉学教授。他专心研究疼痛, 已被我聘为CASA荣誉会员(因为他是美国麻醉学月刊编委)。左志义(佛吉尼亚大学医学院)和蒋延东(Vanderbilt 范德比尔特大学医学院)二教授均被我聘为荣誉会员, 因为他们也是美国麻醉学月刊编委! 张劲军著《中国疼痛学科发展先驱陈秉学教授》。周海峰、林永健和黄国杰可谓“中山医大三侠”, 德才双馨, 堪为人表。

刘恒意 (Henry Liu MD) 和黄建宏 (Jeffrey Jianhong Huang MD) 曾任CASA月刊主编, 呕心沥血, 竭尽全力。黄建宏教授终于在2/25/2016, 为月刊获得正式出版号码 (ISSN, International Standard Serial Number, 国际标准刊号)。

刘恒意教授才智杰出, 不仅学问好, 而且活动能力极强! 对CASA的发展, 居功至伟!

不久前, 黄建宏教授组织团队将美国斯坦福大学医学院手术室应急手册翻译成中文, 这对中国麻醉接轨世界有巨大的促进! 我发文盛赞, 并鼓励所有CASA会员在自己的手机上下载: 1. 斯坦福大学医学院手术室应急手册; 2. 哈佛大学医学院儿科麻醉应急手册!

CASA月刊, March 2017, 刊登张晓彤医师著《十年》。李娟医师 (Beth Israel Deaconess Medical Center) 嘉文《我的美国行医之路, 启航了》。

《留学生之歌》新版歌词, 载入CASA月刊, April 2017, Volume 3 Issue 4。

CASA与时俱进。加州王清 MD PhD 医师(北京协和医学院八年制毕业), 2003年在旧金山美国麻醉年会期间与大学同学的丈夫

-李鸥一起为CASA订制了会旗，与我一起成功主持了CASA周六晚中、美、加拿大华人麻醉交流聚会。她率先组织CASA网群并任群主，该群团结凝集了中美麻醉医师们：1) 有力地促进CASA会员交流；2) 中美麻醉界携手共进！

2018年，美国华人麻醉医学会（CASA）月刊更上一层楼。主编曹锡清（北京协和医学院八年制，美国华盛顿中心医院）医师，是研究诊治恶性高热专家，而且博学，才艺非凡！活动能力强，人脉很广！她将CASA月刊办成了精品！曹锡清医师在CASA史册上，新立一丰碑！

18. 小城故事喜和乐 看画听歌收获多

K城有几老，故事多多。姚宁生先生早年台湾海军官校毕业，来美后到IBM工作至退休，曾多次去中国旅游，总是盛赞中国。他长期订阅唐德刚的《传记文学》。我定期向他借阅，终于理顺了民国，最喜欢的文章是上海陈存仁医师回忆录。罗英昌父亲早年留学日本，曾任民政厅长，国大代表，他台大商学毕业，先后在纽约市-田纳西求学。与一农夫女儿-同学南希（音乐老师）成家立业，在IBM升至经理后退休。马雪雅，西北人，父亲黄埔军校毕业后，去西安任警察局长。西安事变后官升三级！为何？因为蒋委员长去西安前，他曾发一密电（电报）：西安时局不稳，慎行！陈文忠（Winston Chen）祖籍浙江海宁陈府。母：黄慕兰，“共产党的活档案”，电视剧《风筝》记述了她部分人生。她曾任中共机要员，坐过国民党监牢，大陆易权后，因曾与潘汉年工作而被捕，进北京秦城监狱。陈先生父亲去了台湾，母亲进了秦城监狱。1965年在上海高中毕业，不允升大学，只好去了新疆建设兵团。吃过大苦。可他心宽。大陆改革开放后，其舅父（泰国侨领）请求柴泽民大使照顾外甥。陈离新疆欲返回上海，可又卡在湖北黄石。后来，其父托人为他办好加州大学伯克利分校，来美读了大学计算机专业，来IBM工作至退休。齐雅明，青岛人。有两位姑姑，1949年前已被美国中西部一大学录取。可大陆与美断交。1972年，尼克松总统访华后，二姐妹仍单身再联系昔日录取之大学。问：可否今日再来留学。美国学校领导因其故事感动，立即答应欢迎。二姐妹中年来到美国中西部完成学习均毕业了！齐雅明本是青岛市一工人，来美学习计算机，到IBM工作。雅明兄齐雅格学习音乐指挥，现任科罗拉多市交响乐团指挥。

曾听前辈讲过两个故事：

一九五几年，一位台湾青年大学毕业，服了兵役，乘船到西雅图入美国。因为需要等待火车去芝加哥大学，便进入附近一家电影院。进去一看他为难了：影院中心好座位均是白人群。影院最后两排均是黑人们。他不知道自己该坐那里方妥。于是，他坐在通道上了。一会儿，查票员来问：为何不去座位。这位留学生悄声说：的确不知道该坐好区还是到最后排去？查票员问他：你从哪里来？要到哪里去？贵干？留学生如实说：正要去芝加哥大学读博士。查票员立即果断地说：你应去中央好区坐！学生连连道谢！

一九六几年，美国亚特兰大市，一位华裔教授从波士顿去参加专业年会。走向卫生间时，突然看到醒目字体：白人，另一边标示：有色人种。教授看到有色人种排队很长、很慢。希望去白人卫生间，可又惧怕被撵。犹豫不定，忽然见一白人服务员走来，便上前询问：去哪个卫生间合适？那位白人女服务员问到：你贵干？教授说：哈佛大学医学院教授，医师。女服务员说：你应去白人卫生间！此时，1965年左右！种族隔离仍如此！

我们几乎每年均要招待一些师生朋友们。朱秀轩和邱卫乔，李刚和山华，胡宗元和崔铮，吴关和刘玉芳，董建明和黄宇锋全家，虞积仁老师和女儿虞洪及女婿宫歆，邓辉老师和女儿，刘恒意和李孟蓉，潘怡和先生，周海峰和李辛勤，李迺曦和全欣，陈国纲和林华，谢燎阳和陈晓飞，王长征和朱雅丽全家，田惠荣及家人，唐越和朱丽娟全家，黄希松，冯鸿辉和曾赛环，谢京丰和梅虹，郎文生和徐扬，朱强，任延方，左仪，刘宏伟，彭红，岳林，房东坡和程显英，刘强和李琳，王劲和马宁，刘承鲁和潘静波全家，刘宝钢和殷树花全家（少爷：刘金野有著作），陈华和林兰全家，于晓方和闻钟秀，赵浩生和今泉智慧....

我们曾去约翰霍普金斯大学拜访于晓方教授全家和山华教授全家。去麻省 Andover（Phillips Academy）拜访巢卫与刘合玲，谢仲凉和吴音，周海峰和李辛勤家，李迺曦和全欣，陈国纲和林华，王长征和朱雅丽，冯鸿辉和曾赛环.....

友谊需要不断培养和珍惜！

那一代留学生们多爱听邓丽君的歌：邓丽君歌真善美千万学子得
济慰。庄奴歌词如诗如画，丹尼曲美不胜收。邓丽君（1953 -
1995）歌声欢声笑语，又如诉如泣——神曲！从小盒软带、光
盘、至数码，百听不厌，促人向上！因为常在车里放歌，烙印于

孩子们心头。让那不朽的歌声经久绕梁！

过去三十余年，许多大陆留学生正是沿着台湾留学生前辈们的足
迹奋力向前。



(王清摄影作品, Pinnacles National Park, California)

WISONIC公司简介

华声医疗，成立于2013年，总部位于中国深圳；是一家拥有完全自主知识产权，集研发、制造、营销为一体的中国国家高新技术企业。华声是全球POC专科应用领域一线品牌，以临床专业专科精准诊疗为基础，提供“专科专用”的产品和服务。华声拥有“一核两翼”——其核心是云端医疗服务，两翼是生命信息支持、智能超声影像。目前，华声与全球顶级医院共同建成培训基地，与多所院校建立技术前沿的联合实验室。华声致力于服务全球，聚焦全球中高端医疗用户；进口替代，走进国内400多家三级医院；出口升级，产品出口100多个国家和地区。华声用智慧科技，呵护更多生命健康需求，让更多人分享专属生命关怀。

产品介绍：

针对麻醉科室，华声目前有2款核心麻醉专用超声，信息如下：

指南针 (英文型号名：Navi S)：秉承着“专科专用”的理念，经过大量的市场调研，了解了一线客户的痛点和需求，华声医疗于2016年推出了业内首款麻醉疼痛专用彩超——指南针。指南针以其19寸超大的全触屏设计、全面的穿刺解决方案，很好地克服了传统超声操作复杂、穿刺针显影不清等问题。通过近几年的市场推广、专家体验、学术合作等，在麻醉疼痛领域，目前在中国市场占有率稳居第一，在国际上也逐渐树立口碑。打破了进口品牌在相关领域的传统垄断局面。

北斗 (英文型号名：Labat SP)：2019年，华声医疗推出了首款麻醉专科AI智能超声——北斗。作为一款高端彩超，北斗采用了HOLO BEAM 全息平台，无需调节焦点，图像更清晰。同时，基于强大的硬件平台，北斗智能识别神经、血管及各类组织，配合专业的教学软件，使得超声下组织识别更为快速、简单，也极大地缩短了入门医生的学习曲线。此外，北斗的激光导航功能更是产学研合作的成果之一，创新地解决临床穿刺定位困难的问题。



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