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New Progress in the Analysis of Hardness, Morphological Characteristics and Intervention Strategies of renal, gallbladder and salivary gland calculi

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Abstract：Kidney stones, gallstones and salivary gland stones are all common diseases of the urinary system, digestive system and salivary glands. Their hardness, morphological characteristics and formation are closely related. In recent years, with the continuous development of medical imaging technology, materials science and minimally invasive techniques, significant progress has been made in the analysis of physical properties, etiology and intervention measures of kidney, gallbladder and salivary gland stones. Therefore, this review will take renal, gallbladder and salivary gland calculi as the starting point, analyze the hardness, morphological characteristics and formation mechanisms of different types of calculi, explore the application effects of different intervention measures in patients with renal, gallbladder and salivary gland calculi, and provide a basis for clinical diagnosis and treatment.

Key Words：Kidney stones Gallstones; Salivary gland calculi Stone hardness; Morphological characteristics; Intervention strategy Clinical diagnosis and treatment

Foreword

The common feature of kidney, gallbladder and salivary gland stones is that mineral deposits form solid structures. However, due to the different locations of the stones, as well as differences in anatomical positions, compositions and environments, the hardness and morphology of different types of stones vary[1]. With the continuous development of medical technology, the intervention for kidney, gallbladder and salivary gland stones has evolved from open surgery to minimally invasive treatment. However, recurrence still relies on dietary adjustments and drug intervention, lacking precise targeted intervention[2]. The hardness of kidney stones is related to their composition, and the hardness determines the method of lithotripsy. Gallstones are relatively soft, while pigment stones are relatively hard. Hardness affects the difficulty of endoscopic stone removal and the selection of instruments[3]. The hardness of salivary gland stones varies greatly, which affects the power selection and operation skills of endoscopic laser lithotripsy. Kidney, gallbladder and salivary gland stones are closely related to the pathogenesis. Kidney stones come in various forms and are associated with metabolic abnormalities, infections or drug factors. The morphology of gallstones can be single, multiple or sandy, which is related to the imbalance of bile composition and abnormal gallbladder contraction function[4]. Salivary gland calculi can be spindle-shaped, long columnar or round in shape, which is related to duct anatomy, salivary flow rate and component deposition. This review will start with kidney, gallbladder and salivary gland calculi, analyze the hardness, morphological characteristics and formation mechanisms of different types of calculi, and explore the application effects of different intervention measures in patients with kidney, gallbladder and salivary gland calculi. The review is as follows.

1 The hardness, morphological characteristics and formation mechanisms of different types of stones

1.1 Hardness, morphological characteristics and formation mechanism of kidney stones

1.1.1 Relationship between the hardness characteristics and Composition of kidney Stones

The hardness of kidney stones is mainly determined by their mineral composition, and the Mohs hardness varies significantly among different types of stones. Calcium oxalate stones (accounting for 70.0%-80.0%). This type of stone has a Mohs hardness of 3.5 to 4.0, is hard in texture, and has a rough surface with mulberry-like or star-like protrusions. Calcium oxalate stones are formed by the secondary phase transformation of calcium oxalate hydrate crystals to create a dense structure. Their hardness stems from the strong covalent bonds between the crystals. Therefore, in clinical practice, extracorporeal shock wave lithotripsy (ESWL) can be used for intervention, which can break the stones with high energy[5]. Calcium phosphate stones (accounting for 6%-9%). Calcium phosphate stones have a Mohs hardness of 3.0 to 3.5. Their surfaces are rough and stratified, filling the renal pelvis in a antler shape. This type of stone is mainly caused by the supersaturated deposition of calcium phosphate crystals in alkaline urine. The crystals are loosely arranged but have a relatively high overall hardness. (3) Uric acid stones (accounting for 6%-10%). The Mohs hardness of uric acid stones is 2.5 to 3.0. The stones are brittle in texture, smooth on the surface, and yellow or brownish in color. This type of stone is easily dissolved by alkaline urine due to the supersaturated crystallization of uric acid in acidic urine, and the hydrogen bond interaction between crystals is relatively weak. For stones with a diameter of less than 2cm, ESWL intervention can achieve good results. Combined with potassium citrate to alkalize urine can promote the dissolution of stones[6]. (4) Infectious stones (accounting for 5%-10%). The Mohs hardness of the calculi is 2.0-2.5, with a loose texture and a dendritic or dirty gray color. This is mainly due to the decomposition of urea by urease-producing bacteria to generate ammonia, which leads to an increase in urine pH and the precipitation of magnesium ammonium phosphate and magnesium ammonium phosphate. Moreover, the intervention effect of ESWL is poor.

1.1.2 Morphological Characteristics and Pathological Relationship of Kidney Stones

The shape of kidney stones can reflect their formation environment and dynamic process. Common shapes include: round/oval, antler-shaped stones and stratified

stones, etc. (1) Round/Oval stones. This type of stone has a smooth surface and a diameter greater than 1cm. It mainly grows freely in the renal tubules and is less affected by the flow rate of urine, making it easy to be excreted through the ureter (this type of stone is seen in patients with hypocalcemia). (2) Antler-shaped stones. Antler-shaped stones fill the renal pelvis and calyces, with a rather complex shape. This is mainly due to the stagnation of urine in the kidneys, which causes the deposition of crystals in the collecting system[7]. (3) Stratified stones. Fluctuations in urine components lead to intermittent crystal deposition, which can reflect long-term metabolic disorders. The cross-section of this type of stone is in a concentric circle structure.

The morphology of kidney stones is the result of the combined effect of genetic, metabolic, anatomical and microbial factors, including: metabolic abnormalities, urinary tract obstruction and infection, genetic factors, crystal dynamics, etc. Clinically, corresponding measures should be taken to intervene based on the morphology and hardness of the stones to improve the stone excretion rate.

1.2 Hardness and Morphological Characteristics of Gallstones

1.2.1 Relationship between the hardness Characteristics and Composition of Gallstones

The hardness of gallstones is mainly determined by the minerals or organic components, and the physical properties of different types of stones vary significantly. Cholesterol stones (accounting for 50.0%-80.0%). This type of stone is relatively hard in texture, but lower than that of calcium phosphate stones. Its surface is smooth or multi-faceted, and radiating cholesterol lines can be seen in the cross-section. Cholesterol stones contain a relatively high level of cholesterol. When cholesterol in bile is supersaturated and exceeds the dissolving capacity of bile acids and lecithin, cholesterol crystals precipitate and aggregate to form stones. Meanwhile, obesity, a high-fat diet and abnormal liver metabolism can exacerbate excessive cholesterol secretion[8]. (2) Pigment gallstones (accounting for 37.0%). This stone is soft and fragile in texture, with an irregular shape and a multi-layered cross-section. Stones are

mainly composed of calcium bilirubin salts, with low calcium content. They are often not visible on X-rays. The formation of stones is related to biliary tract infection and cholestasis. (3) Mixed stones (accounting for 6%). This type of stone has a hardness between that of cholesterol stones and pigment stones. It contains relatively more calcium and is mainly formed by the mixture of various components such as cholesterol, pigments and calcium salts. The onset of the disease in patients is often related to the imbalance of bile components, biliary tract infections and cholestasis. Coupled with genetic factors and lifestyle, etc., all can increase the incidence of mixed stones. (4) Black stones (accounting for 6%). This stone is hard in texture, spherical in shape, has no special structure in the cross-section, and its formation is related to the deposition of protein networks. The bilirubin in the body is relatively low, and it appears black.

1.2.2 Analysis of Morphological Characteristics of Gallstones

Gallstones come in various shapes, with common forms including: round/oval, polyhedral, sandy, coral-like and irregular, etc. The formation mechanisms and characteristics of stones of different shapes vary. (1) Round/oval stones. The surface of the stones is smooth, with significant differences in diameter. They are mainly formed by the gradual aggregation of cholesterol crystals and cause relatively little friction on the gallbladder wall. They are more commonly seen in patients with cholesterol stones. (2) Polyhedral calculi. Stones have sharp edges and corners, are cubic or rectangular in shape, and have rough surfaces or indentations. The formation of stones is often related to the complex effects of various components in bile, such as cholesterol, calcium salts, and bile pigments. Moreover, stones are relatively hard in texture, making it difficult for drugs to dissolve them. (3) Sand-like stones. This type of stone is composed of fine particles, forming irregularly and resembling silt. The formation of stones is related to excessive bile composition and abnormal gallbladder contraction function, and can be excreted through drug dissolution[9]. (4) Coral-like stones. The stones have a branched structure, similar to coral, and are formed by the fusion of multiple small stones. They may be related to the special shape of the gallbladder or abnormal bile flow. This type of stone is relatively fragile in texture and

prone to fragmentation. (5) Irregular stones. The shape of the stones is irregular, their size varies, and their composition is relatively complex. In clinical treatment, the size, location and complications of the stones should be fully considered.

1.3 Hardness, morphological characteristics and formation mechanism of salivary gland calculi

The hardness of salivary gland stones is mainly determined by their mineral composition, and they are usually quite hard in texture. The hardness characteristics of this type of stone include: (1) Main components. The stones are mainly composed of calcium salts, among which calcium phosphate accounts for 70.0% to 75.0% and calcium sulfate 10.0% to 15.0%, and they also contain small amounts of trace elements such as magnesium, iron, copper and zinc, which makes the stones relatively hard. (2) Physical properties. Salivary gland stones are relatively hard in texture. Some soft stones can be crushed by hand like sand and mud, but most stones need to be treated through medical means. Due to the above-mentioned hardness characteristics, the stones are prone to blocking the ducts, causing obstruction of saliva secretion, leading to glandular swelling and pain. In clinical treatment, endoscopic surgery or extracorporeal shock wave lithotripsy can be selected for treatment[10]

Salivary gland stones come in various forms and are related to their formation location and composition. (1) Shape ①Intraductal calculi. It often takes the shape of a spindle, a long column, a circle or an irregular shape, which is adapted to the shape of the catheter. ②Stones within the gland. It is located deep within the gland, and its shape may be more irregular, influenced by the structure of the gland. ③ Submandibular gland calculi. It is mostly circular at the axial stalk Angle, which is related to the anatomical location of the gland. (3) Size. The size of the stones varies significantly. For smaller stones, sand grains can be inserted, and it is difficult to distinguish them with the naked eye. Larger diameter stones such as jujube seeds; (4) Color and surface. Salivary gland stones are mainly yellow, but light yellow and brown can also be seen. The longer the formation time, the darker the color. The

surface of a stone can be smooth or uneven, which is often related to the deposition pattern in which the stone forms[11].

2 The application effects of different intervention measures in patients with kidney, gallbladder and salivary gland calculi

2.1 Application of Drug Therapy in Renal, Gallbladder and Salivary Gland Calculi

(1)Kidney stones. Targeted inhibition of crystallization. Targeting glycolic acid oxidase can reduce the level of calcium oxalate crystals. Phase III clinical trials have shown that it can significantly decrease oxalic acid excretion in urine. Meanwhile, phytochemical components can inhibit calcium oxalate crystallization by regulating oxidative stress and reduce crystallization aggregation by chelating calcium ions. Jia Yinqiang et al[12].pointed out in a review that calcium oxalate stones of the kidney are common diseases in the urinary system. Citric acid and its derivatives can affect metabolites in urine, inhibit crystal growth, change the crystal phase, regulate protein activity, and have a strong antioxidant effect, providing a reference for the oral drug treatment of kidney stones. (2) Gallstones. Ursodeoxycholic acid is suitable for patients with stone diameters less than 1.5cm by dissolving cholesterol stones and inhibiting cholesterol synthesis. Probiotic preparations can reduce the production of secondary bile acids and lower the recurrence rate of stones by regulating the intestinal flora. Chen Jing et al[13].70 patients with liver and gallbladder damp-heat type gallstones as the subjects. The control group was treated with modified Sanhuang Paishi Decoction for oral administration, while the observation group was treated with ursodeoxycholic acid in combination. The results showed that the modified Sanhuang Paishi Decoction combined with ursodeoxycholic acid could improve the symptoms and serum biochemical indicators of patients with gallstones, help enhance the gallbladder contraction function of patients, and had high safety, which was conducive to the recovery of patients. (3) Salivary gland calculi. For patients with secondary infections, penicillins or cephalosporins can be selected to help them control inflammation. Pilocartin can promote the excretion of small stones through secondary salivary secretion.

2.2 The effect of minimally invasive surgery in the treatment of kidney, gallbladder and salivary gland stones

For those who do not respond well to drug stone expulsion, minimally invasive surgical intervention can be considered. Kidney stones. For kidney stones with a diameter greater than 2cm, percutaneous nephrolithotomy can be selected for treatment. Stones are removed under direct vision through the renal puncture channel, and the stone clearance rate reaches 90.0%. For patients with subrenal calyx stones, flexible ureteroscopic laser lithotripsy can be selected for intervention. Through natural cavity operation, it causes less trauma and has a faster recovery. Hu Xiaojian et al[14]. took 103 patients with kidney stones of 2cm or less as the subjects and divided them into the flexible ureteroscopic lithotripsy group and the tubeless minimally invasive percutaneous nephrolithotomy group according to different treatment methods. All patients were given corresponding surgical treatment interventions. The results showed that different surgeries could achieve good effects in patients with kidney stones. However, the tubeless minimally invasive percutaneous nephrolithotomy has less trauma, milder postoperative stress and inflammatory responses, fewer postoperative complications, and can shorten the postoperative recovery time. (2) Gallstones. Laparoscopic cholecystectomy is the gold standard surgical procedure for patients with gallstones. It is suitable for symptomatic gallstones and has few postoperative complications. Endoscopic retrograde cholangiopancreatography is suitable for common bile duct stones. Stone removal through duodenoscopy can reduce the rate of open surgery. Wang Xiaobing[15] took 90 patients undergoing gallstone surgery as the subjects and randomly divided them into two groups of 45 cases each by the envelope method. The control group was treated with laparoscopic combined with choledochoscopy surgery, while the observation group was treated with laparoscopic combined with retrograde pancreatic ductal angiography. The results showed that laparoscopic combined with retrograde pancreatic ductal angiography could achieve good effects for patients with gallstones and had a shorter postoperative recovery time. (3) Salivary gland calculi. For patients with salivary gland stones, laser ablation under direct vision of salivary gland

endoscopy can preserve glandular function and is suitable for patients with intraductal stones. Meanwhile, patients with this type of stone can also be treated with intraoral incision stone removal. Stone removal through an incision in the oral mucosa has a relatively small impact on the patient's appearance and can improve patient compliance.

2.3 Preventive Measures for kidney, Gallbladder and Salivary gland Stones

Although drug and surgical treatments can achieve good results in patients with renal, gallbladder and salivary gland calculi, the drawbacks of different intervention measures are obvious. Kidney stones. For patients at high risk of kidney stones, dietary intervention should be strengthened, with increased fluid intake and restrictions on foods high in oxalic acid, salt and purine. For patients with recurrent calculi, strengthen the 24-hour urine analysis of the patients and supplement potassium citrate or allopurine in a targeted manner. (2) Gallstones. For obese patients, weight loss can reduce the saturation of cholesterol in bile. In daily life, they should avoid prolonged fasting to promote the emptying of the gallbladder. (3) Salivary gland calculi. Remind the patient to brush their teeth regularly and use mouthwash to reduce bacterial colonization. Chewing sugar-free gum or lemon slices can promote saliva secretion.

3. Conclusion

In conclusion, there are differences in the hardness and shape of kidney, gallbladder and salivary gland stones, and they are closely related to the composition and formation of the stones. Therefore, when conducting clinical intervention, appropriate treatment methods should be selected in combination with the type of stones, the patient's condition, and medical resources, etc. Through multidisciplinary collaboration, different types of stones will develop towards precision, minimally invasive and individualized directions, which will help improve the quality of life of patients. In subsequent research, the core pathways of different types of stones can be deeply analyzed, such as the role of osteopontin in kidney stones and the influence of intestinal flora in gallstones. Actively develop catheters that can degrade stones or drug coatings to reduce surgical trauma. Deep learning is applied to analyze the

imaging features of calculi, assist in diagnosis and prognosis assessment, and achieve a favorable prognosis.

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