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CFD Analysis of the Choledynamic Flow Characteristics of a Patient with Gallbladder Carcinoma

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ABSTRACT

Gallbladder carcinoma (GBC) is a rare malignancy with a low detection rate due to non-specific symptoms, complicating early diagnosis and treatment. This study aims to improve pre-operative and post-operative surgical analysis using patient-specific CFD analysis. CT scan images of a male patient with GBC were segmented using 3D Slicer software, and the biliary tree geometry was imported into ANSYS Workbench for fluid and solid meshing. The mechanical properties of the biliary tree and the rheological properties of bile were determined, with an LRN k-ω model used for simulating the gallbladder refilling stage. Results indicate that unhealthy bile flows slower than healthy bile, suggesting a link between obstructed bile flow and tumors or stones. Tumor-induced blockages cause pressure accumulation in the gallbladder neck, unlike the minimum pressure in healthy cases. These findings highlight the complex interplay between bile rheology, tumor development, and pressure dynamics, suggesting the model's potential use in surgical planning.

1. Introduction

Gallbladder carcinoma is a rare form of malignancy that constitutes half of the reported cases of biliary cancer [1]. According to the report of the International Agency for Research on Cancer from 2020, gallbladder carcinoma ranks 28th or about 0.19% of the new cases of cancer detected in the Philippines. Detection for gallbladder carcinoma is challenging due to the rarity of the detected symptoms. For gallbladder cancer in its initial stages, surgery is still the recommended course of treatment. Suitable surgical strategies are chosen based on the primary tumor's anatomical position, precise preoperative stage, and stringent control over surgical indications to achieve the best surgical outcome. Surgery removes tumors and obstructions so the patient's gallbladder performance will revert to its healthy function [2]. Furthermore, after the operation, a surgeon cannot anticipate changes in the body's recovery toward normal functionality (bile's daily flow rate, biliary system segment pressure, wall shear stress, etc.).

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It is crucial to perform a physiological and mechanical description of the behavior of the human biliary system to comprehend the causes of diseases [3]. Moreover, CFD simulation will make predicting the postoperative outcome before surgery easier as it offers significant advantages in research by reducing time and resource expenditure, enabling precise control of input parameters, and predicting process behavior throughout the simulated domain [4]. In the case of CFD analysis, investigating the gallbladder performance and the impact on bile choledynamics is a critical task [5]. It is well known that one of the most effective ways to address complex medical issues is through patient-specific computational fluid dynamics (CFD) analysis [3]. Patient-specific CFD simulations have been done previously by Al-Atabi *et al.,* [6] on the flow of bile in the human cystic ducts, Kuchumov *et al.,* [7] on the non-Newtonian flow of pathological bile, Kuchumov *et al.,*[5] on the gallbladder refilling of a healthy human, Kuchumov *et al.,* [3] on the FSI model of bile flow, and Peng *et al.,*[8] on the bile dynamics within the biliary tract.

Previous studies regarding gallbladder refilling and emptying stages have focused on FSI simulations and using the Windkessel model. Although there have been studies comparing healthy bile with lithogenic bile [3, 5], there is still a lack of study in CFD simulations on bile choledynamics, especially in patients with gallbladder carcinoma. Additionally, existing CFD simulations for bile flow often employ turbulence models like k-ε or k-ω [6, 9]. However, these models may be overly complex for the potentially low Reynolds number flows encountered in diseased states like gallbladder carcinoma. The Low Reynolds Number (LRN) k-ε model offers advantages in such scenarios as it is designed explicitly for low Reynolds number flows [10], a condition that may arise due to altered bile viscosity or flow restrictions in a diseased gallbladder. Standard k-ε or k-ω models can struggle with these low Reynolds number conditions, potentially leading to inaccurate predictions. The LRN k-ε model incorporates modifications to account for the damping effect of walls on turbulence in low-flow situations [11]. This can provide more reliable results than standard models when simulating bile flow in a diseased gallbladder.

In this study, the researchers aim to create a CFD simulation using a patient-specific geometry of a gallbladder cancer patient. The bile rheology will be determined, and its effects on the velocity and pressure distributions during the refilling stage will be investigated. The LRN $k-\omega$ model will be used to solve the CFD simulation. While Fluid-Structure Interaction (FSI) simulations offer a more comprehensive approach by coupling fluid dynamics with structural mechanics, they can be computationally complex, especially when dealing with biological tissues. In this study, the primary focus is on understanding the impact of bile rheology on flow patterns within the biliary system. Comparisons between healthy bile and bile in patients with gallbladder carcinoma will also be determined.

The study will not focus on the determination of wall shear stress distributions, von Mises stress distributions, and the influence of viscosity. Comparisons with other models and the validation study will not be conducted due to time constraints. Additionally, this is a single-patient study, which inherently limits the generalizability of the findings to a broader population. Future research with a larger patient group could provide more comprehensive insights into how bile flow patterns and their association with gallbladder carcinoma vary across individuals.

Even though the dynamics of bile flow within the biliary system and the characteristics of the gallbladder have already been examined independently by other researchers, the use of patient-specific models is necessary for providing better care. This will help doctors during preoperative and post-operative procedures. Thus, it is essential to perform patient-specific CFD simulations to assess how fluid flow affects the surrounding tissues and vessels and vice versa [3]. Developing and implementing new technological strategies to anticipate and prevent postoperative difficulties is

vital. The paper will address this by creating an optimum pre-surgical and post-surgical plan that uses computational fluid dynamics (CFD) analysis.

2. Methodology

2.1 Patient-Specific Geometry

The CT scans of a male patient with gallbladder carcinoma were obtained legally from the Cancer Imaging Archive. They were imported to the 3DSlicer 5.6.1 software (Massachusetts Institute of Technology, Cambridge, MA, USA), as shown in Figure 1. Afterward, the biliary system was segmented using total segmentation. Recognizing the critical role of segmentation accuracy in model fidelity, the researchers implemented additional steps to refine the initial segmentation. Careful consideration was given to the resolution of the medical images to ensure proper distinction between anatomical structures. Furthermore, 3D Slicer's advanced segmentation algorithms were utilized alongside manual refinement of segmented regions to enhance the overall accuracy of the biliary tree model. Once segmentation was complete, the resulting geometry was exported for further processing within ANSYS Workbench (ANSYS, Inc., Canonsburg, PA, USA).

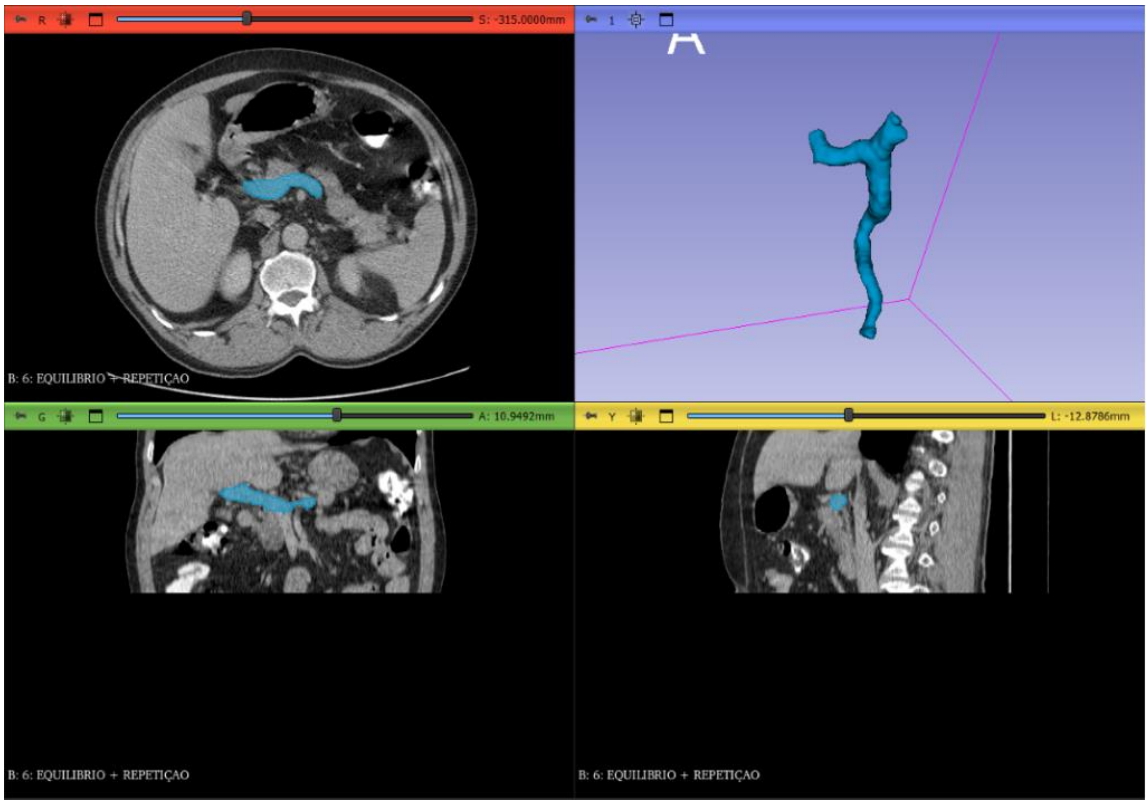

Fig. 1. CT scan images (axial, coronal, and sagittal) of a male patient with gallbladder carcinoma and the generated 3D model.

2.2 Meshing

ANSYS Fluent was used for both the solid and fluid domain meshing. The numerical solution's convergence process was investigated in a patient's bile flow who had gallbladder malignancy. Throughout the convergence investigation, many mesh modifications in finite elements were considered. The minimal size of the element for either fluid or solid mesh was calculated using the structure's smallest overall size and the optimal mesh size to be chosen. The mesh's convergence

result demonstrated no variance in the results, indicating that the mesh had no impact on the outcomes. There were 51469 elements and 16173 nodes in the solid and fluid meshes. Polyhedra elements were mapped into a solid mesh (Figure 2). The fluid mesh's minimum size was established at 0.3 mm.

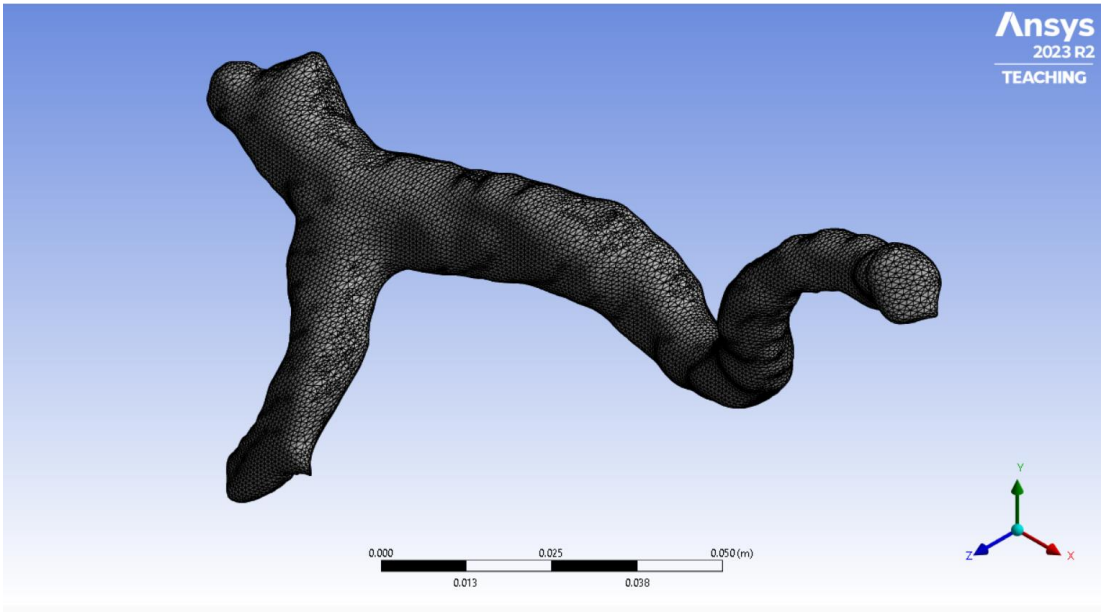

Fig. 2. Meshes mapped with polyhedral elements

2.3 Mechanical Properties of the Biliary Tree

The biliary tree's mechanical characteristics were taken from Kuchumov *et al.,* [3] according to the biliary tree ducts' experimental inflation testing. The outcomes adhered to the Mooney-Rivlin model, as shown in Eq. (1), and demonstrated that the constitutive parameters for c_{10}, c_{01}, and d were 6.34 kPa, 0.88 kPa, and 0.38 Pa^{-1}, respectively.

$$E_{s.e.d.} = c_{10}[I_1 - 3] + c_{01}[I_2 - 3] + \frac{1}{d}[J - 1]^2 \quad (1)$$

Where $E_{s.e.d.}$ is the strain energy – density function, I_1 and I_2 are the initial and secondary Cauchy–Green invariants in terms of tensor deformation, J is the gradient of elastic deformation's determinant, c_{10} and c_{01} are the constitutive parameters, and d is the incompressibility of the biliary tree.

2.4 Rheological Properties of the Bile Fluid

The lithogenic anomaly enhances activity in the protein, which raises the amount of biliary sterol secreted from the canalicular membrane of hepatocytes into the biliary tree. Gallstones are caused by this hypersaturation of cholesterol [12]. This increases the viscosity of bile, which causes it to behave differently from a Newtonian fluid. It is invalid for this study to presume that the bile fluid flows in a non-Newtonian behavior as represented by the Carreau model because gallstone development did not occur. To depict the biliary characteristics, a Newtonian model was instead selected. Based on the research of Luo *et al.,* [13] and Ooi *et al.,* [14], the constitutive parameters

were determined to be 1020 kg/m^3 for the density and a viscosity of 0.001 Pa-s, assuming a Newtonian fluid for the biliary fluid.

2.5 Governing Equations

The Navier-Stokes equation can be used to define the equations for the conservation of momentum and mass for an incompressible fluid. This is conveyed as:

$$\nabla \cdot u = 0, \tag{2}$$

$$\rho_f \left(\frac{\partial u}{\partial t} + \Big((u - u_g) \cdot \nabla\Big) u\right) = -\nabla p + \nabla \cdot \tau, \tag{3}$$

Where ρ_f is the density of the bile fluid, u is the vector of the bile fluid's velocity, u_g is the moving coordinate velocity, p is the bile fluid's pressure, and τ is the stress deviator tensor. Through the strain rate tensor, the tensor is connected to the velocity and can be expressed in terms of cartesian coordinates as:

$$\tau_{ij} = \eta \left(\frac{\partial v_i}{\partial x_j} + \frac{\partial v_j}{\partial x_i}\right) \tag{4}$$

Where x_i and x_j are the i^{th} and j^{th} spatial coordinates, v_i and v_j are the velocities of the bile fluid in the direction of the *i* and *j* axis respectively, η is the shear-strain rate, and τ_{ij} is the j^{th} element of the stress applied to the elements of the bile fluid's faces perpendicular to the *i*-axis.

For the solid body, the momentum conservation equation is expressed as:

$$\nabla \cdot \sigma_s = \rho_s \dot{u_g}, \tag{5}$$

Where ρ_s is the density of the biliary tree, σ_s is the stress tensor, and $\dot{u_g}$ is the biliary tree's local acceleration.

The study of Vassilevski *et al.,* [15] and Amabili *et al.,* [16] described the hyper-elasticity of the blood vessels. While biliary ducts and blood vessels share some anatomical similarities, their functional differences necessitate a closer look at their material properties. Both structures experience repetitive mechanical stress and strain, suggesting potentially similar biomechanical responses. However, limited research has directly investigated the hyper-elasticity of human biliary ducts. Studies like Luo *et al.,* [17] highlight the scarcity of human data, relying primarily on animal models. Jian and Wang's [18] work on canine bile ducts demonstrates a baseline stress distribution and a decline in elastic modulus from the common bile duct to the hepatic duct, suggesting regional variations in elasticity. These findings from animal models support the possibility of hyper-elastic behavior in human biliary ducts. The stress and strain relationship for hyper-elastic materials is expressed as follows:

$$\sigma_s = \frac{\partial E_{s.e.d.}}{\partial \epsilon} \tag{6}$$

Where $E_{s.e.d.}$ is the strain energy-density function as represented by the Mooney-Rivlin equation, ϵ is the strain tensor, and σ_s is the stress tensor.

Despite the anatomical and functional similarities with blood vessels and the suggestive evidence from animal studies, the classification of human biliary ducts as hyper-elastic materials requires further validation. The lack of direct human data and the observed heterogeneity in animal models emphasize the need for future experimental investigations. These human biliary tissue sample studies would offer crucial data to confirm the hyper-elastic assumption and establish more precise material property information.

2.6 Boundary Conditions

For the solid domain, the ends of the extrahepatic biliary tree were assumed to be fixed supports, which caused restrictions. Thus, there is no displacement and no rotation in all the axes.

The gallbladder refilling stage was presented in this study. Bile exits the liver and gallbladder simultaneously during the gallbladder refilling process. The pressure gradient-induced bile flow mechanism in the biliary channels from the gallbladder to the duodenum is represented by the LRN $k-\omega$ model [19].

$$\frac{\partial k}{\partial t}+u_j\left(\frac{\partial k}{\partial x_j}\right)=\tau_{ij}\left(\frac{\partial u_i}{\partial x_j}\right)-\beta\cdot k\omega+\frac{\partial}{\partial x_j}\left[(v+\sigma_k v_T)\left(\frac{\partial k}{\partial x_j}\right)\right] \tag{7}$$

Where k is the turbulence kinetic energy, u is the mean velocity, x is the position vector, v is the kinetic molecular viscosity, v_T is the kinetic eddy viscosity, and ω is the pseudovorticity. The values of β and σ_k are 1 and 0.5, respectively.

The Reynold's number represents the flow characteristics of the bile fluid. It is defined as:

$$N_{Re}=\frac{\rho Dv}{\mu}, \tag{8}$$

Where ρ is the bile fluid's density, D is the average inner diameter of the biliary ducts, v is the bile fluid's velocity, μ is the bile's dynamic viscosity, and N_{Re} is Reynold's number.

The observed flow was laminar as the value of Reynold's number does not exceed 2100. This is consistent with the findings of several authors [3,14,20]. In addition, the average gallbladder refilling time, with a mean bile volume of 35 ml, is approximately 30 minutes, under studies of Al-Atabi *et al.,* [6] and Behar [21]. Moreover, the laminar flow assumption and its change are adequately gradual to make steady-state conditions a basis for the CFD analysis.

The average velocity of 0.003 m/s was applied as velocity at inlet 1. At the outlet, the pressure was assumed to be equivalent to the duodenal pressure of 960 Pa [22]. Since only integrated parameters for mean flow rate were discussed, the pulsatile flow inlet and pressure exit were left out. There were studies in the literature on intra-operational measurements ranging from bile flow out of the liver [23] to pressure in the duodenum [22]. The model assumes that if we know the patient-specific flow and pressure profiles that vary with time, we should apply pulsatile boundary conditions at the input and output.

3. Results

3.1 Velocity Distribution

The CFD analysis of the bile flow of a patient with gallbladder carcinoma reveals insights into how it differs from a healthy state. Based on the results, the maximum velocity was found to be 0.426 cm/s, as shown in Figure 3, which is much slower compared to a healthy bile flow of 2.6 cm/s as based on the study of Kuchomov *et al.,* [3]. This suggests that there is a potential link between the sluggish bile movement and cancer tumors or stones causing obstructions. Interestingly, the location of the maximum velocity remains in the cystic duct (inlet 2), as seen in healthy individuals.

Velocity plummets in the hepatic duct when the bile is obstructed, possibly aligning with the formation stones in the low-flow areas. This effect goes beyond slowing things down; low-flow areas reconfigure the flow paths within the gallbladder neck, further disrupting the flow dynamics. The swirling in the cystic duct was seen throughout the refilling stage (Figure 3). The disruptions to the normal choledynamics of the cystic duct, which generate acceleration after the stenosis zone, are responsible for the greatest velocity of the bile fluid found in the cystic duct. Additionally, the variations in velocity values for a patient-specific geometry are visible, especially in the case of gallbladder malignancy.

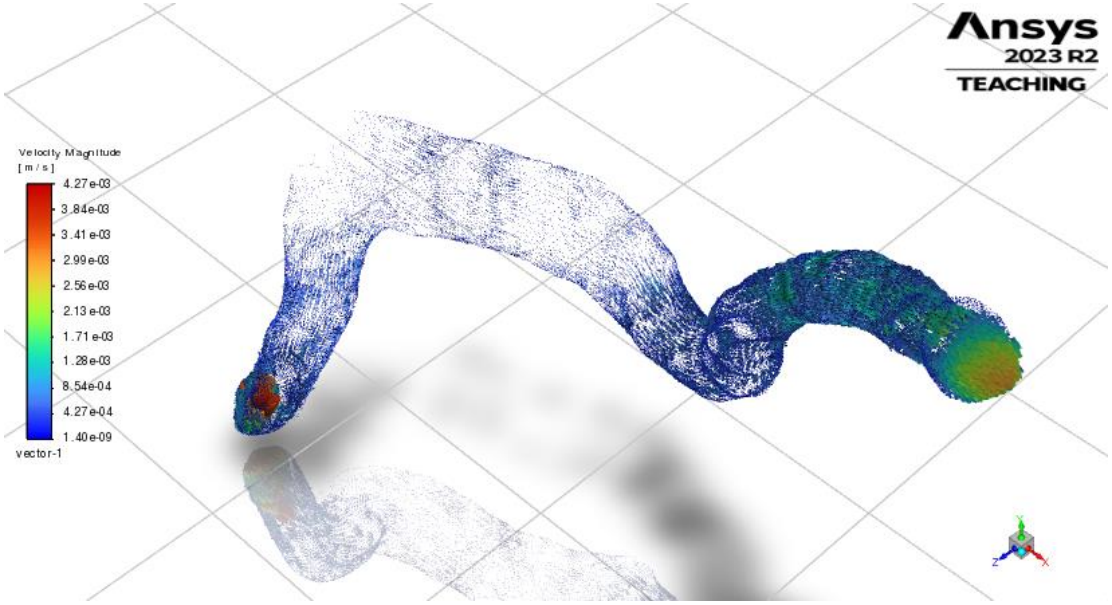

Fig. 3. Velocity distributions during gallbladder refilling stage

3.2 Pressure Distribution

Unlike the minimal pressure observed in a healthy gallbladder neck, the presence of tumors that cause obstructions creates a pressure build-up in this region (Figure 4). This contrasts with the other areas of the system, where the pressure remains relatively unchanged except for the common bile duct. The pressure hovers around 960 Pa in this region, consistent with established medical data. Interestingly, the bile fluid of a patient with gallbladder carcinoma does not seem to exert much influence on the pressure distribution compared to the healthy bile. The real culprit is the change in geometry caused by the obstructions, specifically the narrowing of the cystic duct lumen. This construction acts like a dam that forces pressure to rise in localized zones. These findings suggest a complex interplay between bile composition, tumor formation, other obstructions, and resulting

pressure dynamics within the gallbladder. The presence of obstructions played a crucial role in altering the pressure landscape.

The biliary system's pressure drop, flow rate, and flow resistance strongly correlate with gallbladder motor activity [20]. The vagus, splanchnic nerves, and a number of hormones, including cholecystokinin (CCK), are among the neurohormonal processes that intimately integrate the motor functions of the gallbladder and biliary tract with the rest of the digestive system. CCK release regulates the gallbladder's contraction and bile discharge into the duodenum during fasting and digesting times [24]. Gallbladder function may be a significant indicator of the results of careful waiting or surgery because the symptoms often are thought to result from the constriction of the gallbladder [25].

Because bile viscosity increases in pathological cases, the bile of a patient with gallbladder cancer demonstrates that pressure values are higher in healthy bile flow scenarios; the extrahepatic biliary tree experiences an increase in pressure levels when an obstruction is present. This is somehow related to the medical evidence presented in the paper of Csendes *et al.,* [26].

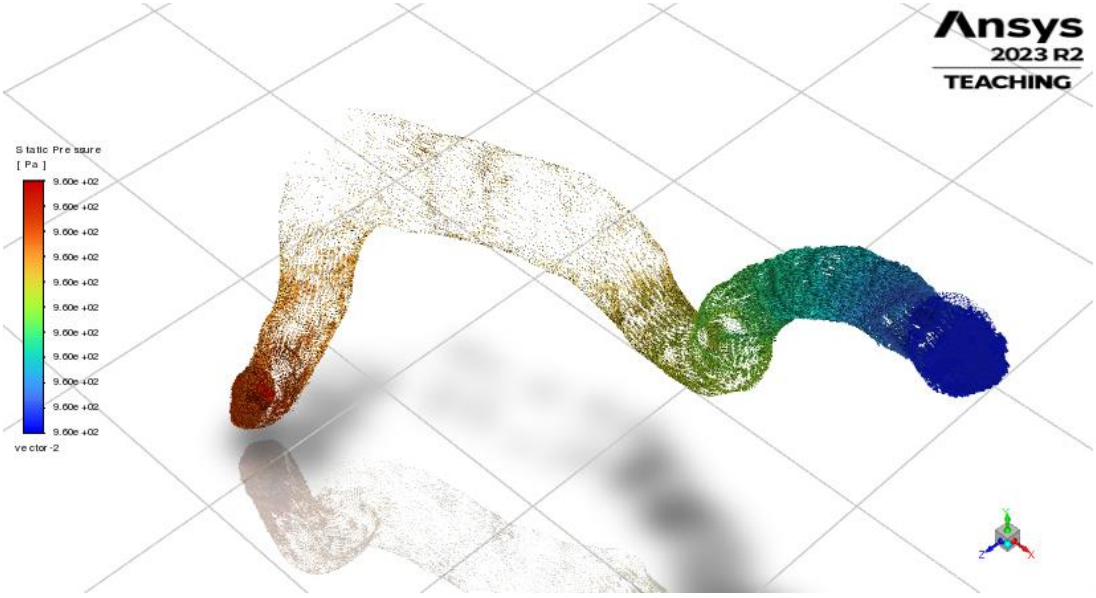

Fig. 4. Pressure distributions during the gallbladder refilling stage

3.3 Clinical Applications

Non-invasive diagnostic and therapeutic numerical techniques in modern surgery enable the estimation of the biomechanical operations within the human anatomy. This situation makes it more likely to be used to enhance current and new novel, individualized techniques for predicting and treating conditions. Specifically, there is an increasing requirement for use in biliary system surgery applications [3].

Gallbladder surgeries are reported to cause 15% Incidence problems following surgery [27, 28]. Among the causes are the examination of subjective experience and the absence of customized biomechanical models to interpret different surgical methods.

Developing and implementing new technological strategies to anticipate and prevent postoperative difficulties is vital. One such strategy could be to create optimum pre-surgical and post-surgical plans that use computational fluid dynamics (CFD) analysis (Figure 5).

With the help of a suggested model of the biliary system, difficulties can be predicted and avoided by evaluating choledynamics in healthy and diseased settings and by numerically assessing bile flow

following gallbladder surgery. With the help of this paper's findings, a surgeon can assess a patient's preoperative gallbladder cancer and post-operative bile flow features.

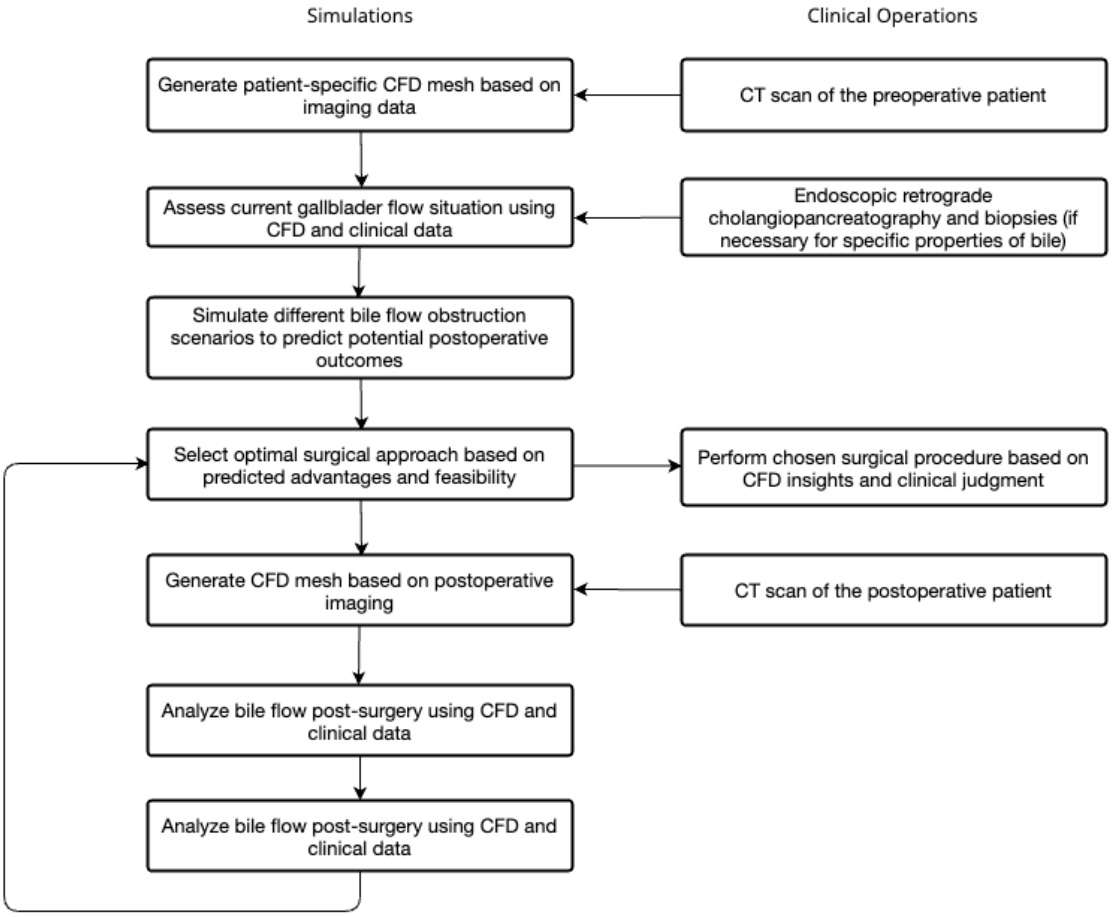

Fig. 5. Schematic diagram of a pre-surgical and post-surgical strategy employing CFD simulations

4. Conclusions

Using the LRN $k-\omega$ model, the impact of bile pathology on the pressure and velocity distributions in the extrahepatic biliary tree unique to a patient was examined during the refilling stage. Additionally, a comparison was made between a patient's healthy bile and the bile of a patient who was diagnosed with gallbladder carcinoma. The CFD research revealed that the maximum velocity of the unhealthy bile was much slower than that of the healthy bile, indicating a possible connection between the obstructed bile flow and cancerous tumors or stones. As observed in healthy individuals, the highest velocity remains situated in the cystic duct. The highest bile fluid velocity in the cystic duct is caused by disturbances to the regular choledynamics of the duct, which produce acceleration after the stenosis zone. There is also an accumulation of pressure in the gallbladder neck when tumors induce blockages, as opposed to the minimum pressure found in a healthy gallbladder neck. Compared to healthy bile, the bile fluid from a patient with gallbladder cancer doesn't seem to impact the pressure distribution. The obstruction-induced geometric change causes the result. Notably, the lumen of the cystic duct becomes narrower. The pressure is forced to increase in certain areas because of the geometry. Overall, these results point to a complicated interaction between the rheology of the bile, the development of tumors and other blockages, and the pressure dynamics that arise inside the gallbladder. The pressure landscape was modified mainly by the existence of obstructions. The bile of a patient with gallbladder cancer illustrates that pressure values are higher

in healthy bile flow situations because bile viscosity increases in pathological circumstances. When an obstruction is present, the pressure within the extrahepatic biliary tree increases. Consequently, the suggested model might be used in medical procedures to assess the conditions surrounding surgical methods.

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