Acta of Bioengineering and Biomechanics
Vol. 15, No. 4, 2013

Original paper
DOI: 10.5277/abb130402

Modelling of the pathological bile flow in the duct with a calculus

ALEX G. KUCHUMOV[1]*, YURIY I. NYASHIN[1], VLADIMIR A. SAMARCEV[2], VASILIY A. GAVRILOV[2]

[1] Department of Theoretical Mechanics, Perm National Research Polytechnic University, Perm, Russia.
[2] Department of General Surgery #1, Academician E.A. Wagner Perm State Medical Academy, Perm, Russia.

The aim of the present paper is to develop an analytical model for description of the pathological bile flow in the major duodenal papilla duct with a calculus. The problem is separated into two parts. The first part deals with determination of bile behaviour and constitutive relation parameters of the pathological bile. The viscosity vs. shear rate, the viscosity vs. time, and shear stress vs. shear rate dependences are obtained for different types of bile taken from patients of different age and sex. As a result, the approximation of curves described by the Casson equation was obtained. It was shown that the pathological bile is a thixotropic non-Newtonian fluid.

The second part is directly related to modelling of the bile flow in the duct with a calculus. As a result of solving the problem, the bile velocity profile, flow rate vs. time, and bile pressure vs. calculus radius were obtained. The dependences obtained may play an important role in the assessment of an indication to operation.

Key words: *biliary system, bile flow, non-Newtonian fluid, Vater's papilla*

1. Introduction

The most common diseases of the biliary system are cholelithiasis, which is associated with the formation of stones in the gallbladder and bile ducts, and choledocholithiasis (stones found in the common bile duct as a result of migration from the cystic duct). If the diameter of the stone is less than the diameter of the cystic duct, there is a possibility for calculus moving from the gallbladder into the common bile duct or major duodenal papilla, which leads to inflammation of the duct and blocks the ingress of bile into the duodenum (papillary stenosis) [1], [2].

Long-standing common biliary duct (CBD) stones lead to varying degrees of papillary stenosis [1], [3]. The latter could predispose to new stone formation because of the damaged CBD mucosa and varying degrees of stasis. The extent and speed of this inflammation may be different – from a small swelling wall until its destruction and the bubble burst [3]–[5].

The sphincter of Oddi at Vater's papilla is an important regulator of biliary and pancreatic flow into the duodenum. The papillary stenosis is a state when the flow from biliary ducts and pancreatic channel is disturbed [6], [7].

It has been shown that a significant number of surgically obtained biopsies of the papilla in these patients have histological changes, for example, fibrosis, inflammation, hypertrophy of the sphincter, etc., [3]. Shortly, the stenotic changes of the papilla have two important correlates: narrowing of the sphincteric ampulla by stones, and thickening of the transampullary septum. Most patients with papillary stenosis have choledocholithiasis and postoperative pain experience [8]–[10]. Coexistence of choledocholithiasis, dilated CBD and papillary stenosis would theoretically predispose the cholecystectomised patient to new stone formation and pancreatitis.

* Corresponding author: Alex G. Kuchumov, Department of Theoretical Mechanics, Perm National Research Polytechnic University, 29 Komsomolskii Prospect, 614990, Perm, Russia. Tel: +7(342)-2-39-17-02, fax: +7(342)-2-198-067, e-mail: kychymov@inbox.ru
Received: November 1st, 2012
Accepted for publication: May 10th, 2013

According to Edemskiy et al. [4], acute and chronic inflammatory changes in Vater's papilla occur in 100% of patients with gallstone disease, and in 89.6% of patients with recurrent pancreatitis.

Three degrees of the major duodenal papilla cicatricial stenosis were highlighted by Vinogradov [3].

Cicatricial stenosis of the papilla caused wedged calculus was first described only in the late 19th century. In 1926, Dell-Vail and Donovan [6] reported stenosing papillitis, not associated with cholelithiasis and later use of intravenous and operating cholangiography, manometry and radiometric studies have led Mallet-Guy [11], Caroli [12], Hess [5] and others to identify the wide spread of the disease, especially in cholelithiasis. Among patients with biliary tract pathologies (such as «choledocholithiasis» [a disease characterized by migration of stones from the cystic duct into the common bile duct]), Hess [5] highlighted papillary stenosis in 50% of cases (total number of patients was 1220).

Whilst the anatomical and physiological aspects of the human biliary system have been studied extensively, a little is known about flow mechanics in the system, especially in pathological states such as papillary stenosis [9], [13]–[15].

Ooi et al. [16] performed a detailed numerical study on flow in two- and three-dimensional cystic duct models. The cystic duct models were generated from patients' operative cholangiograms and acrylic casts. The pressure drops in these models were compared with that of an idealised straight duct with regular baffles or spiral structures.

Li et al. [15] developed numerical fluid–solid interaction models of normal bile flow in the cystic duct. An influence of spiral Heister's valve was accounted for. After that, an experimental work was also carried out to validate the computational fluid dynamics predictions in the simplified ducts [13] and real patient duct [14].

In [17], the possibility was shown of creating more difficult models of biliary system in norm and pathology in the framework of international megaproject «Virtual Physiological Human» [18]–[20].

This project deals with creation of digital representation of the human body as a single complex system based on the patient's data, which is unique. The information about systems, organs, and tissues interacting with each other will allow medical workers to select methods of treatment on the basis of patient-specific features. For example, the knowledge of reaction of the patient's organism to current drug will allow avoiding medical errors during the treatment and even save the patient's life.

The necessity to consider the human body as a complex multi-scale and multi-functional system gives us the possibility to create realistic predictive models based on obtained experimental and clinical data and approved by medical practice [19], [21], [22]. Integration of data collected on these hierarchical levels with help of multi-disciplinary research will give valuable information for the healthcare development.

This paper deals with only one step towards total description of processes occurring in the biliary system, namely modelling of the pathological bile flow in the duct with a calculus.

The paper is arranged in the following sequence. Section 2 contains anatomical summary on the biliary system as a whole. Anatomical and physiological aspects of the sphincter of Oddi functioning are presented. Section 3 contains results of the measurement of pathological bile rheological properties. The dependences of viscosity on shear rate, the viscosity changes with time, as well as shear stress versus shear rate dependences were obtained for different types of bile from patients with the same pathology, but of different age and sex. The parameters of the Casson equation are presented as a result of curve approximation. Section 4 deals with solution of the problem of the bile flow in Vater's papilla duct with a calculus, thus the problem of mathematical physics is solved.

2. Materials and methods

2.1. Anatomy

Biliary system is designed to release a bile (secret of the liver) containing many metabolic products into the duodenum [23]. Biliary system includes the gallbladder, biliary tract (cystic duct, hepatic duct, CBD, and a system of sphincters (Fig. 1) [24].

The right and left hepatic ducts exit from the liver and form the common hepatic duct. Cystic duct is an extension of the neck of the gallbladder. Common bile duct is formed by the merger of common hepatic and cystic ducts [25], [26].

The human gallbladder is a thin-walled, pear-shaped sac which measures approximately 7–10 cm in length and ~3 cm in width. Its average storage capacity is 20–30 ml. The human cystic duct is approximately 3.5 cm long and 3 mm wide and merges with CBD [24].

The distal segment of the common bile duct enters the pancreas. Common bile duct opens into the duo-

denum in the major duodenal papilla, which is surrounded by the sphincter of Oddi [3].

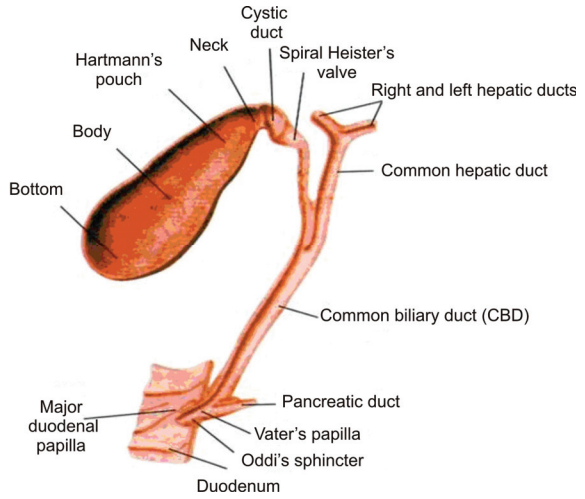


Fig. 1. Anatomy of the biliary system

There are several variants for the connection of the common bile duct with the pancreatic duct in the major duodenal papilla (Fig. 2).

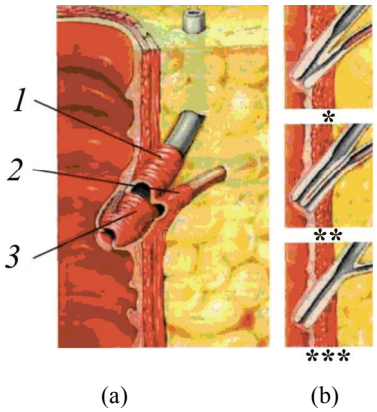


Fig. 2. Anatomical elements of the sphincter of Oddi:
(a) general anatomy (1 – sphincter of the common bile duct,
2 – sphincter of pancreatic duct,
3 – sphincter of major duodenal papilla ampoule),
(b) different variants of the papilla's ampoule structure
(* – bifurcation in the major duodenal papilla ampoule,
** – parallel arrangement of ducts,
*** – bifurcation before ampoule [28])

Sphincter regulates the flow of bile into the intestine and prevents a dumping of duodenal contents into the bile ducts. In the area there are two types of sphincter motor activity: basal pressure and phase of the periodic contractile activity. Basal pressure is responsible for regulating the outflow of secretion of bile and pancreatic ducts [8], [27].

The calculi formation in the biliary system is a complex process due to the influence of many physiological, biochemical, and biomechanical factors such as an irregular meal, metabolism, the effect of duct wall elasticity on a bile flow, the gallbladder contractile function, etc.

One of the dangerous complications of the presence of calculi in the biliary system is a blockage of the duct by a calculus (stone) in the major duodenal papilla zone [2]. As a result, disruption of the normal flow of bile from the liver to the duodenum results in the increase of the jaundice risk. Moreover, the bile components (cholesterol, bile acids, etc.), which are harmful for humans, are accumulated in the human body [29].

The present paper contains biomechanical analysis of the pathological bile flow in the duct with a calculus to obtain choledynamics flow characteristics to assess individual daily loss of bile for each patient and the influence of the calculus size on the pressure in the major duodenal papilla, which may be an indication for surgery in the major duodenal papilla in order to decompress the duct.

2.2. Bile properties tests

To solve the problem, firstly, it is necessary to carry out an experimental study of the bile rheological properties to determine the constitutive relation parameters for the subsequent modelling.

Samples of bile were taken from the gallbladder of the patient during the cholicystoectomy (removal of the gallbladder) (the gallbladder bile) or as a result of the biliary tract drainage (the duct bile) conducted at the Department of General Surgery, Medical Faculty, Perm State Medical Academy and the Emergency Surgery Department at Perm City Clinical Hospital No. 4. To determine the rheological characteristics of biological fluids, the "Physica MCR 501" rheometer was adopted. Rheological tests were conducted at +37 °C.

To find the flow characteristics of the bile, the geometry of a "cone–plate" was used, because it was determined that such geometry is best suited for the investigation of low viscous fluids by the rotational viscometer.

During the experiment, about 15 ml of the sample was poured on the working surface of the rheometer's plate. The initial and final values of shear stress were set, as well as the experiment time. In the case of the gallbladder bile, the experiment time was equal to 160 s, in the case of the duct bile 180 s. The range of shear stresses ranged from 1 to 5 Pa, as it was shown that in the range from 0 to 1 Pa, the convergence of the results is low. The experiments were performed in the different shear stress ranges to get

more information about liquid behavior. The initial load applied to the bile was 1, 2, 3, and 4 Pa. After application of initial load and choice of the experiment time, the following dependences were obtained, namely viscosity vs. shear stress, shear stress vs. shear rate, viscosity vs. time.

The aim of the experiment was to determine the type of the pathological bile from the point of view of fluid mechanics, to consider of differences in the rheology of the gallbladder bile and the duct bile samples, as well as to determine constitutive relation parameters for subsequent simulation of the bile flow.

The Casson equation is used to extrapolate the dependences describing the flow curve of the material,

$$\sqrt[p]{\tau} = \tau_0 + \eta \cdot \sqrt[p]{\dot{\gamma}} \qquad (1)$$

where τ is the shear stress, $\dot{\gamma}$ is the shear rate, τ_0 is the limit shear stress, η is the Casson viscosity, p is the Casson degree.

The Casson equation is commonly used to describe the rheological behavior of fluids (bio-fluids), particularly the blood [30] and the synovial fluid [31].

2.3. Pathological bile flow in a duct with a calculus

Let us now consider the case of pathological bile flow as a non-Newtonian bile in Vater's papilla duct (a duct length is l, a radius is b) with a calculus (a radius is a) as a laminar flow between coaxial cylinders (p_e) (Figs. 3, 4).

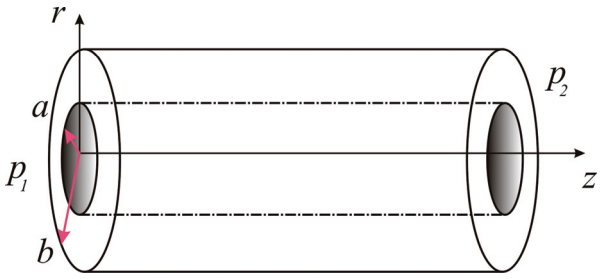


Fig. 3. Problem geometry

The Casson equation with parameters taken from Table 2 was used. As the index of the shear stress and the shear rate is close to 1, so we take it equal to 1 in the subsequent computations. The problem is close to classical Casson's problem [32], nevertheless, different geometry, initial conditions, and Navier–Stokes equations are adopted here.

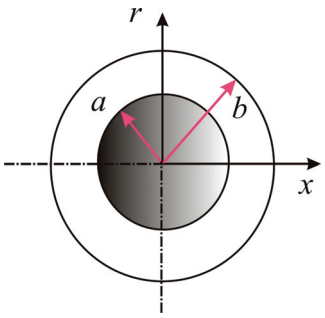


Fig. 4. Duct cross section ($r = b$) with a calculus ($r = a$)

The Navier–Stokes equation takes the form [33]

$$\rho\left(\frac{\partial \vec{V}}{\partial t} + \vec{V}\cdot\nabla\vec{V}\right) = -\nabla p + \overline{\nabla}\cdot\vec{\tau}. \qquad (2)$$

As the bile flow is uniaxial and laminar, then $\vec{V} = (\vec{V}_r, \vec{V}_\theta, \vec{V}_z) = (0,\ 0,\ \vec{V}_z)$. Thus, equation (2) in cylinder coordinates takes the form

$$\rho\frac{\partial V_z}{\partial t} = -\frac{\partial p}{\partial z} + \frac{1}{r}\frac{d}{dr}(r\tau_{rz}). \qquad (3)$$

Substituting (5) in (6) and considering that degree is close to 1, one can obtain

$$\frac{\partial V_z}{\partial t} = -\frac{1}{\rho}\frac{\partial p}{\partial z} + \frac{0.72}{\rho r} + \frac{6.23}{\rho r}\frac{d}{dr}\left(\left(r\cdot\left(\frac{\partial V_z}{\partial r}\right)\right)\right).$$

Let us imply the following notifications

$$V_z = w;\quad C = -\frac{1}{\rho}\frac{\partial p}{\partial z};\quad k = \frac{0.72}{\rho};\quad l^2 = \frac{6.23}{\rho}.$$

Therefore, the problem takes the form

$$\begin{cases} w_t = l^2\Delta w + f(r),\ a < r < b,\ 0 < \varphi < 2\pi,\ t > 0, \\ w|_{t=0} = w_0, \\ w|_{r=a} = 0, \\ w|_{r=b} = 0, \end{cases}$$

where $f(r, t) = C + \dfrac{k}{r}$; w_0 is the initial velocity of the bile in the duct.

The division of variables $w(r, t) = T(t)R(r)$ gives

$$T'(t)R(r) = T(t)\cdot\frac{l^2}{r}\left[\frac{\partial(R(r))}{\partial r} + r\frac{\partial^2 R(r)}{\partial r^2}\right]. \qquad (4)$$

Dividing both parts into $T(t)R(r)$, one can obtain

$$\frac{T'}{T} = \frac{l^2}{r}\frac{R'}{R} + l^2\frac{R''}{R} = -\mu. \qquad (5)$$

The solution of equation (5) is

$$T = w_0 e^{-\mu t}. \tag{6}$$

The other part of equation takes the form

$$\frac{l^2}{r}\frac{R'}{R} + l^2\frac{R''}{R} = -\mu.$$

$$r^2R'' + rR' + \frac{\mu}{l^2}r^2R = 0.$$

Let $\frac{\mu}{l^2} = \lambda$. Thus,

$$r^2R'' + rR' + \lambda r^2R = 0. \tag{7}$$

The general solution of equation (7) is

$$R(r) = C_1J_0(\sqrt{\lambda}r) + C_2N_0(\sqrt{\lambda}r), \tag{8}$$

where $J_0(\sqrt{\lambda}r)$ and $N_0(\sqrt{\lambda}r)$ are the Bessel functions of the zero order of the first and second kinds, respectively.

After finding C_1 and C_2, one can obtain

$$R_m(r) \equiv \frac{J_0(\sqrt{\lambda_m}a)}{J_0(\sqrt{\lambda_m}b)}\{J_0(\sqrt{\lambda_m}r)N_0(\sqrt{\lambda_m}b) - J_0(\sqrt{\lambda_m}b)N_0(\sqrt{\lambda_m}r)\}.$$

Finally, the solution takes the form

$$w = \sum_m \frac{f_m R_m(r)}{l^2\lambda_m} + \sum_m \left(\Phi_m - \frac{f_m}{l^2\lambda_m}\right)e^{-l^2\lambda_m t}R_m(r),$$

where

$$\Phi_m = w_0\left(\frac{S}{\sqrt{\lambda_m}}\{bJ_1(\sqrt{\lambda_m}b) - aJ_1(\sqrt{\lambda_m}a)\} - \frac{B}{\sqrt{\lambda_m}}\{bN_1(\sqrt{\lambda_m}b) - aN_1(\sqrt{\lambda_m}a)\}\right),$$

$$f_m = SC\int_a^b J_0(\sqrt{\lambda_m}r)rdr - BC\int_a^b N_0(\sqrt{\lambda_m}r)rdr + \frac{2Sk}{\sqrt{\lambda_m}}\sum_{k=0}^{\infty}\{J_{2k+1}(\sqrt{\lambda_m}b) - J_{2k+1}(\sqrt{\lambda_m}a)\} - \frac{2Bk}{\sqrt{\lambda_m}}\sum_{k=0}^{\infty}\{N_{2k+1}(\sqrt{\lambda_m}b) - N_{2k+1}(\sqrt{\lambda_m}a)\},$$

$$S = \frac{J_0(\sqrt{\lambda_m}a)N_0(\sqrt{\lambda_m}b)}{J_0(\sqrt{\lambda_m}b)}, \quad B = J_0(\sqrt{\lambda_m}a), \quad \lambda_m$$

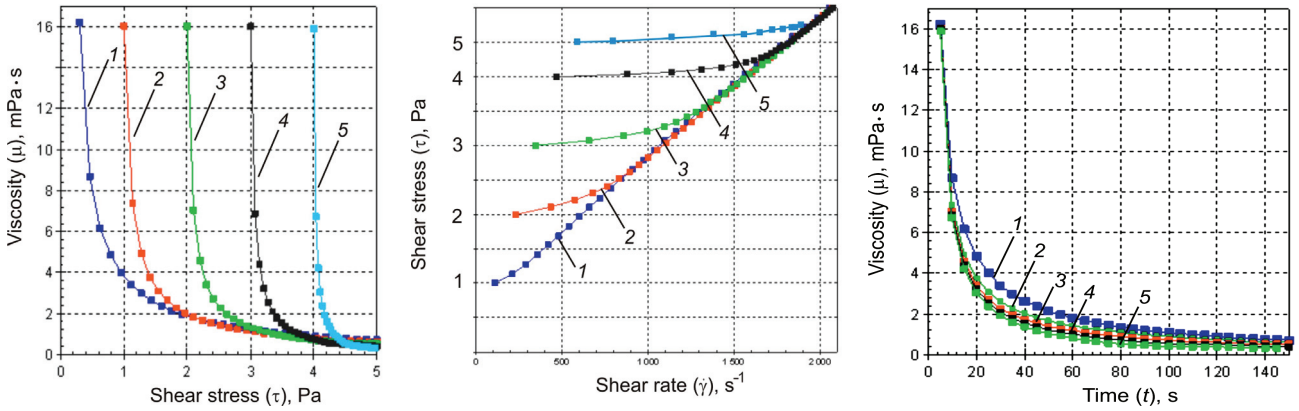
are the solutions of equations (8).

3. Results

3.1. Experimental results

3.1.1. Duct bile

Figure 5 (a)–(c) shows the dependences obtained for the duct bile. From these relationships, it is clear that the bile has the properties of non-Newtonian thixotropic fluid (a liquid that becomes less viscous when stirred).



(a) (b) (c)

Fig. 5. Rheological curves adopted for the duct bile in the range of shear stress: 1 – 0.3–5 Pa; 2 – 1–5 Pa; 3 – 2–5 Pa; 4 – 3–5 Pa; 5 – 4–5 Pa: (a) dependence of viscosity (μ) on shear stress (τ), (b) dependence of shear stress (τ) on shear rate ($\dot{\gamma}$), (c) dependence of viscosity (μ) on time (t)

From Fig. 5, it can be seen that maximum viscosity is achieved with the initial shear stress, and then curves reach saturation. Such dependence may be due to the destruction of the main structural components of the bile (domains). Originally, the bile consists of a large number of domains, by applying shear stress domains begin to crumble and turn into one large domain; at this time moment, the viscosity curves reach saturation (see Fig. 5a). From Fig. 5b, the nonlinear dependence of the shear stress versus the shear rate is seen, but, it is clear that the curves are close to Newtonian behavior when the initial shear stress and the shear rate increase. From dependence of the viscosity on time (Fig. 5c), it is seen that at the initial shear stress increase, the time destruction of domains decreases. The dynamic viscosity of the duct bile changes in the range of 0.3 mPa to 16 mPa.

Table 1 contains the parameters obtained by extrapolating the curve 1 by the Casson equation.

Table 1. Parameters adopted by the Casson equation extrapolation for duct bile

τ, Pa	τ_0, Pa	η, mPa·s	p
1–5	0.49	0.77	3.17

3.1.2. Gallbladder bile

Figure 6 (a)–(c) shows the dependences obtained for the gallbladder bile. From obtained data, one can conclude that the gallbladder bile, as well as the duct bile is a non-Newtonian fluid. The time of viscosity saturation decreases with an increase of the initial shear stress.

Figures 7 (a)–(b) contain a comparison of bile samples taken from the gallbladder of patients with similar pathology, but different age and sex. From Fig. 7, it is seen that the behavior of the curves of sample 1 and sample 2 is identical, but there is a displacement along the axis, i.e., the curve character is due to the type of bile, and the viscosity depends on several parameters, including the parameters of the patient, such as age and gender.

Dynamic viscosity of sample 1 varies from 23 mPa·s to 6 mPa·s, and sample 2 from 15 Pa·s to 2.5 Pa·s.

According to the data obtained, it can be seen that the gallbladder bile is more viscous than the duct one. Both kinds of the bile are thixotropic fluids.

Tables 2 and 3 contain the parameters obtained by extrapolating the curves by the Casson equation.

Table 2. Parameters adopted by the Casson equation extrapolation for the gallbladder bile sample 1

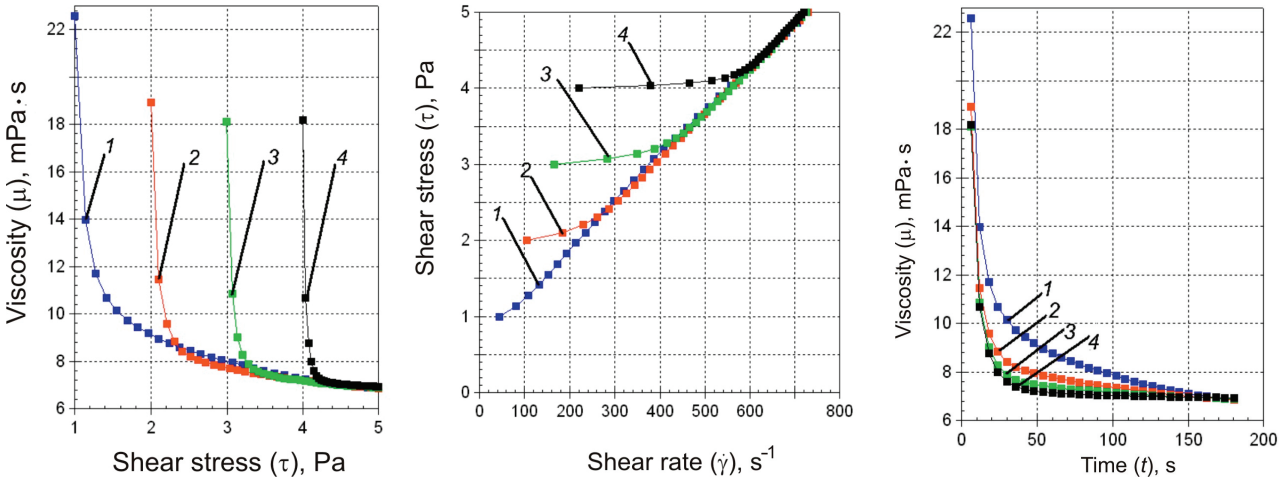
τ, Pa	τ_0, Pa	η, mPa·s	p
1–5	0.72	6.23	0.92

Table 3. Parameters adopted by the Casson equation extrapolation for the gallbladder bile sample 2

τ, Pa	τ_0, Pa	η, mPa·s	p
1–5	0.91	2.84	0.77

3.2. Problem solution results

Parameters adopted during computations of the problem presented in Section 2.3 are given in Table 4.



(a) (b) (c)

Fig. 6. Rheological curves adopted for the gallbladder bile in the range of shear stress: 1 – 1–5 Pa; 2 – 2–5 Pa; 3 – 3–5 Pa; 4 – 4–5 Pa: (a) dependence of viscosity (μ) on shear stress (τ), (b) dependence of shear stress (τ) on shear rate ($\dot{\gamma}$), (c) dependence of viscosity (μ) on time (t)

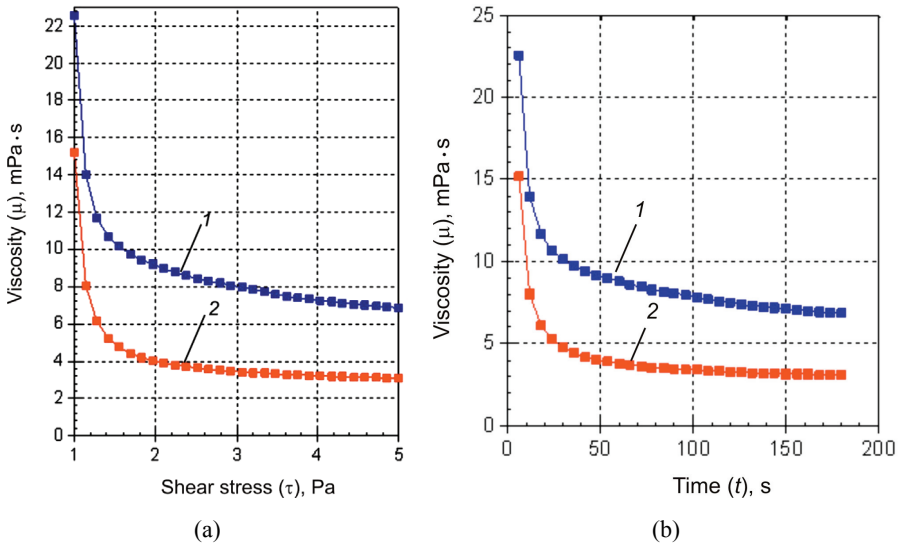


Fig. 7. Comparison of flow curves for samples 1 and 2 at the range of applied shear stress 1–5 Pa: (a) dependence of viscosity (μ) on shear stress (τ), (b) dependence of viscosity (μ) on time (t)

The initial velocity of the bile (w_0) was taken as 5 mm/s; the time t varies from 0 to 250 s. Figure 8 contains the bile velocity profile at arbitrarily taken time moment. From the type of solution, it can be seen that the velocity profile tends to be radial with increasing summands taken in the solution. Figure 9 shows rapid decreasing of the flow rate throughout the time. It can be shown that the situation changes when the calculus dimensions tend to be the same as Vater's papilla duct. With an increase of calculus in the common bile duct, the secretory bile pressure rise occurs, but is not sufficient to provide the amount of bile released in the duodenum increment (Fig. 10).

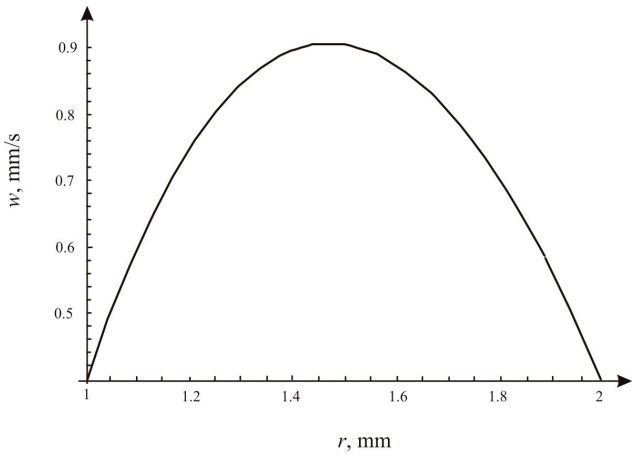


Fig. 8. Bile velocity profile

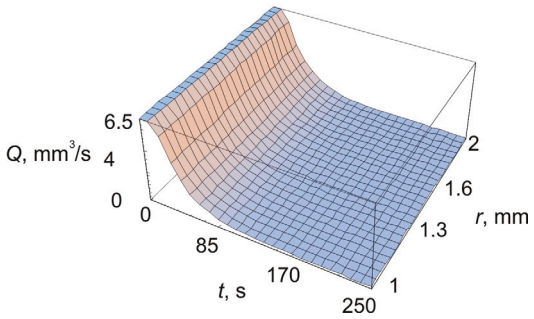


Fig. 9. Dependences of the bile flow rate (Q) on time (t) during flow in Vater's papilla duct with a calculus

Table 4. Biomechanical parameters of the biliary system element (compiled from [17], [34])

Parameter	Value
Diameter of Vater's papilla, mm	4
Length of Vater's papilla, mm	5
Radius of a concrement, mm	1
Bile density, kg/m^3	1020

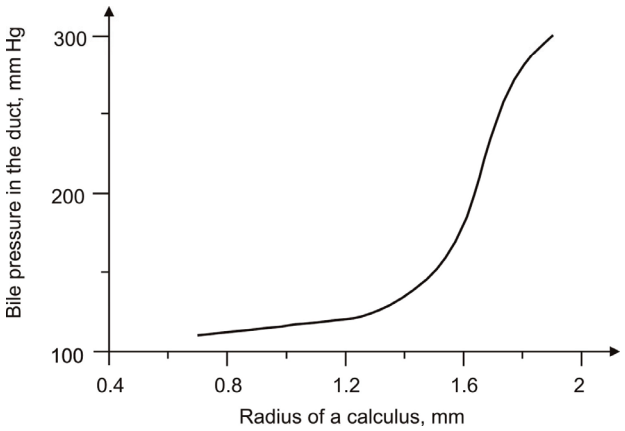


Fig. 10. Dependence of the bile pressure in the duct on the radius of a calculus

4. Discussion

Bio-fluid dynamics modeling has become a widespread tool for surgeons either in cardiology [35]–[37] or other medical areas related with bio-fluids [38]–[40].

The present paper is devoted to the development of an analytical model for description of the pathological bile flow in the major duodenal papilla duct. On the one hand, this model may be considered as a tool for assessing the pathology degree; on the other hand, it may contribute to improve clinical treatment methods.

The problem is separated into two parts.

The first one deals with determination of bile behaviour and constitutive relation parameters of the pathological bile, which requires experimental investigation of bile samples.

The experiments performed showed that pathological bile is a non-Newtonian fluid with thixotropic features. Its behaviour depends on patient's sex, pathology type, and applied loading rate. The difference between duct bile and gallbladder bile was highlighted. It was shown that viscosity of gallbladder bile samples was higher than of duct bile ones, which may be explained by the influence of the different physiological processes taking place in the human gallbladder. The dependence of viscosity on shear rate, the viscosity changes from time to time, shear stress versus shear rate obtained for different types of bile were taken from patients of different age and sex. As a result, the approximation of curves by means of the Casson equation was obtained.

The second part is directly related to the modelling of the bile flow as a non-Newtonian fluid in the duct with a calculus.

On the basis of the problem solved, the dependences of flow resistance were obtained.

The patient-specific mathematical model created allows us to estimate the dynamics of postoperative period and to predict the development of specific complications on the basis of pressure bile data. The information about calculus diameter obtained by the cholangiography gives an opportunity to estimate daily bile amount entering the duodenum.

Moreover, the estimation of bile pressure in the duct is an objective measure of the effectiveness and adequacy of biliary decompression and indication for the operation on the major duodenal papilla and the common bile duct, when the pressure is high and daily bile amount is less than 35% of norm [6], [27].

References

[1] BRUGGE W.R., BRAND D.L., ATKINS H.L., *Gallbladder dyskinesia in chronic acalculous cholecystitis*, Digest. Dis. Sci., 1986, Vol. 31, 461–468.

[2] KRATZER W., MASON R.A., KACHELE V., *Prevalence of gallstones in sonographic surveys worldwide*, J. Clin. Ultrasound, 1999, Vol. 27, 1–7.

[3] VINOGRADOV V.V., *Diseases of the Vater's papilla*, (in Russian), Nauka: Moscow, 1962.

[4] EDEMSKIY A.I., EDEMSKIY D.A., *Major duodenal papilla's pathology*, (in Russian), Surgery Bulletin, 2002, Vol. 7, 35–42.

[5] HESS W., *Die Erkrankungen der Gallenwege und des Pancreas*, (in German), Stuttgart, 1961.

[6] LIANG T.B., LIU Y., BAI X., YU J., CHEN W., *Sphincter of Oddi laxity: an important factor in hepatolithiasis*, World J. Gastroentero., 2010, Vol. 16(8), 1014–1018.

[7] MIYACHI A., KIKUYAMA M., MATSUBAYASHI Y., *Successful treatment of pancreaticopleural fistula by nasopancreatic drainage and endoscopic removal of pancreatic duct calculi: a case report*, Gastrointest. Endosc., 2004, Vol. 59, 454–457.

[8] CICALA M., HABIB F.I., FIOCCA F., PALLOTTA N., CORAZZIARI E., *Increased sphincter of Oddi basal pressure in patients affected by gall stone disease: a role for biliary stasis and colicky pain?*, Gut, 2001, Vol. 48, 414–417.

[9] LI W.G., LUO X.Y., HILL N.A., SMYTHE A., CHIN S.B., JOHNSON A.G., BIRD N.C., *Correlation of mechanical factors and gallbladder pain*, J. Comput. Math. Methods Med., 2008, Vol. 9, 27–45.

[10] RASTOGI A., SLIVKA A., MOSER A.J., WALD R., *Controversies concerning pathophysiology and management of acalculous biliary-type abdominal pain*, Digest. Dis. Sci., 2005, Vol. 50, 1391–1401.

[11] CAROLI J., CORSOS V., *La dilatation congetale des voies biliaris intra-hepatiques*, (in French), Rev. Med. Chir. Mal. Foie, 1964, vol. 39, pp. 1–15.

[12] MALLET-GUY P., ROSE J., *Pre-operative manometry and radiology in biliary tract disorders*, Br. J. Surg., 1956, Vol. 44, 128–136.

[13] AL-ATABI M.T., CHIN S.B., LUO X.Y., *Flow structure in circular tubes with segmental baffles*, JFVIP, 2005, Vol. 12, pp. 301–311.

[14] AL-ATABI M.T., OOI, R.C., LUO, X.Y., CHIN, S.B., BIRD N., *Computational analysis of the flow of bile in human cystic duct*, Med. Eng. Phys., 2012, Vol. 34, 1177–1183.

[15] LI W.G., LUO X.Y., JOHNSON A.G., HILL N.A., BIRD N., CHIN S.B., *One-dimensional models of the human biliary system*, J. Biomech. Eng. – T ASME, 2007, Vol. 129, 164–173.

[16] OOI R.C., LUO X.Y., CHIN S.B., JOHNSON A.G., BIRD N.C., *The flow of bile in the human cystic duct*, J. Biomech., 2004, Vol. 37, 1913–1922.

[17] KUCHUMOV A.G., NYASHIN Y.I., SAMARTSEV V.A., GAVRILOV V.A., MESNARD M., *Biomechanical approach to biliary system modelling as a step towards «Virtual physiological human» project*, Russian Journal of Biomechanics, 2011, Vol. 15, 28–36.

[18] HUNTER P., COVENEY P., BONO B., DIAZ V., FENNER J., FRANGI A., HARRIS P., HOSE R., KOHL P., LAWFORD P., MCCORMACK K., MENDES M., OMHOLT S., QUARTERONI A., SKÅR J., TEGNER J., RANDALL T., TOLLIS I., TSAMARDINOS I., VAN BEEK J., VICECONTI M., *A vision and strategy for the*

virtual physiological human in 2010 and beyond, Philosophical Transactions of the Royal Society A. Mathematical, Physical & Engineering Sciences, 2010, Vol. 368, 2595–2614.

[19] KOHL P., NOBLE D., *Systems biology and the virtual physiological human*, Mol. Syst. Biol., 2009, Vol. 5, 292–298.

[20] VICECONTI M., CLAPWORTHY G., VAN SINT JAN S., *The Virtual Physiological Human – a European initiative for in silico human modelling*, J. Physiol. Sci., 2008, Vol. 58, 441–446.

[21] GRIZZI F., CHRIVA-INTERNATI M., *The complexity of anatomical systems*, Theor. Biol. Med. Model., 2010, Vol. 14, 1–9.

[22] WESTON A.D., HOOD L., *Systems biology, proteomics, and the future of health care: toward predictive, preventative, and personalized medicine*, J. Proteome. Res., 2004, Vol. 3, 179–196.

[23] HOFMANN A.F., *Biliary secretion and excretion in health and disease: current concepts*, Ann. Hepatol., 2007, Vol. 6, 15–27.

[24] KUNE G., *The influence of structure and function in the surgery of the biliary tract*, Ann. R. Coll. Surg. Engl., 1970, Vol. 47, 78–91.

[25] OTTO W.J., SCOTT G.W., RODKIEWICZ C., *A comparison of resistances to flow through the cystic duct and the sphincter of Oddi*, J. Surg. Res., 1979, Vol. 27, 68–72

[26] PITT H., ROSLYN J., KUCHENBECKER S., DOTY J., DENBESTEN L., *The role of cystic duct resistance in the pathogenesis of cholesterol gallstones*, J. Surg. Res., 1981, Vol. 30, 508–514.

[27] CSENDES A., KRUSE A., FUNCH-JENSEN P., OSTER M.J., ORNSHOLT J., AMDRUP E., *Pressure measurements in the biliary and pancreatic duct systems in controls and in patients with gallstones, previous cholecystectomy or common bile duct stones*, Gastroenterology, 1979, Vol. 77, 1203–1210.

[28] HORIGUCHI S., KAMISAWA T., *Major duodenal papilla and its normal anatomy*, Dig. Surg., 2010, Vol. 27, 90–93.

[29] BUCHNER A.M., SONNENBERG A., *Factors influencing the prevalence of gallstones in liver disease: the beneficial and harmful influences of alcohol*, AJG, 2002, Vol. 97, 905–909.

[30] GAVRILENKO S.L., VASIN R.A., SHILKO S.V., *A method for determining flow and rheological constants of viscoplastic biomaterials*, Part I, Russian Journal of Biomechanics, 2002, Vol. 6, 90–96.

[31] SZWAJCZAK E., *Dependence of hyaluronan aqueous solution viscosity on external fields*, Part II, Russian Journal of Biomechanics, 2004, Vol. 8, 89–93.

[32] FUNG Y.C., *Biodynamics: circulation*, Springer-Verlag, 1984.

[33] CURRIE I.G., *Fundamental mechanics of fluids*, McGraw-Hill, 1974.

[34] TEILUM D., *In vivo measurement of the length of the sphincter Oddi*, Endoscopy, 1991, Vol. 23, 114–116.

[35] BLAGOJEVIC M., NIKOLIC A., ŽIVKOVIC M., ŽIVKOVIC M., STANKOVIC G. *Influence of blocks' topologies on endothelial shear stress observed in CFD analysis of artery bifurcation*, Acta of Bioengineering and Biomechanics, 2013, Vol. 15(1), 97–104.

[36] MARIUNAS M., KUZBORSKA Z., *Influence of load magnitude and duration on the relationship between human arterial blood pressure and flow rate*, Acta of Bioengineering and Biomechanics, 2011, Vol. 13(2), 67–72.

[37] TSE K.M., CHIU P., LEE H.P., HO P., *Investigation of hemodynamics in the development of dissecting aneurysm within patient-specific dissecting aneurismal aortas using computational fluid dynamics (CFD) simulations*, J. of Biomechanics, 2011, Vol. 44(5), 827–836.

[38] BEVAN T., CARRIVEAU R., GONEAU L., CADIEUX P., RAZVI H., *Numerical simulation of peristaltic urine flow in a stented ureter*, Am. J. Biomed. Sci., 2012, Vol. 4(3), 233–248.

[39] VAHIDI B., FATOURAEE N., *A biomechanical simulation of ureteral flow during peristalsis using intraluminal morphometric data*, J. of Theor. Biol., 2012, Vol 298, 42–50.

[40] SRIVASTAVA L.M., SRIVASTAVA V.P., *Peristaltic transport of a non-Newtonian fluid (Application to the vas deferens at small intestine)*, Ann. BioMedical Eng., 1985, Vol. 13, 137–153.