

شبكة المعلومات الجامعية







شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



شبكة المعلومات الجامعية

# جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

# قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها على هذه الأفلام قد أعدت دون أية تغيرات



يجب أن

تحفظ هذه الأفلام بعيدا عن الغبار في درجة حرارة من ١٥-٥٠ مئوية ورطوبة نسبية من ٢٠-٠٠% To be Kept away from Dust in Dry Cool place of 15-25- c and relative humidity 20-40%



# بعض الوثائـــق الإصليــة تالفــة



# بالرسالة صفحات لم ترد بالإصل

# Effect of Hemofiltration on Hemostasis during Open Heart Surgery

Thesis
Submitted in Partial Fulfillment of
M.D. Degree in Clinical and
Chemical Pathology

ZYOY

By Siham Assem Ali Barakat M.Sc.(Clin. Path.)

Supervised By

## Prof. Dr. Mohammad El Hindi

Professor of Clinical and Chemical Pathology Banha Faculty of Medicine, Zagazig University

# Prof. Dr. Maha Salah Youssef

Professor of Clinical and Chemical Pathology Banha Faculty of Medicine, Zagazig University

# Assist.Prof. Dr. Mohammad Zakaria

Assistant Professor of Pediatrics
Banha Faculty of Medicine, Zagazig University

Assist.Prof. Dr. Laila El Mahrouky

Assistant Professor of Clinical and Chemical Patholog Banha Faculty of Medicine, Zagazig University

# بسم ولله والرحس والرحيم

"وعلمك ما لم تكن تعلم وكان فضل الله عليك عظيماً "

صدق الله العظيم

(سورةالنساء آيه ١١٣)

# Acknowledgement

It is a great a honour to express my deep gratitude and appreciation to Professor Dr.Mohammad El Hindi, Professor of Clinical and Chemical Pathology, Banha Faculty of Medicine, Zagazig University for his excellent guidance, suggestions and valuable advice.

I am deeply indebted to *Professor Dr. Maha Salah Youssef*, Professor of Clinical and Chemical Pathology, Banha Faculty of Medicine, Zagazig University, for her kind supervision, sincere and valuable help, guidance and support throughout the course of this work.

I am also grateful to Assistant Professor Dr. Mohammad Zakaria,

Assistant Professor of Pediatrics, Banha Faculty of Medicine, Zagazig

University for his sincere help, and cooperation.

I would like also to express my gratitude to Assistant Professor Dr Laila El Mahrouky, Assistant Professor of Clinical and Chemical Pathology, Banha Faculty of Medicine, Zagazig University for her supervision, and helpful guidance.

Lastly but not least I am whole heartedly indebted to my family and colleagues in the Department of Cardiothoracic Surgery and Lab, Ain Shams University, for their perpetual support, assistance and encouragement.

# Contents

# Introduction and Aim of Work

## Review of Literature

Normal Hemostasis	1
- Vascular System	1
- Platelets System	12
- Coagulation Cascade System	23
- Naturally Protective Mechanisms	37
Cardiopulmonary Bypass Inflammatory and Coagulation Response	42
- The Ischaemic Reperfusion Injury	45
- Inflammatory response and Platelet Activation	50
- Coagulation and Fibrinolytic Activation	54
Open Heart Surgery and Blood Transfusion	60
Reduction of Bleeding in Cardiopulmonary Bypass Patients	69
Hemofiltration	72
- Historic Prespective	72
- Hemofiltration and Pediatric Surgery	73
- Basic Physiological Principle	74
Patients and Methods	79
Results	95
Discussion	121
Summary and Conclusion	129
Recommendations	131
References	132

# List of Tables

Table (1a)	Comparison between patients age (yrs.), CPB time (min.) values in the control and hemofilter group.	100
Table (1b)	Comparison between patients' sex in the control and hemofilter group.	100
Table (2a)	Hemoglobin concentration (gm/dl) within the control and hemofilter group.	101
Table (2b)	Comparison between hemoglobin concentration (gm/dl) in the control and hemofilter group.	101
Table (3a)	Hematocrit (%) within the control and hemofilter group.	103
Table (3b)	Comparison between hematocrit (%) in the control and hemofilter group.	103
Table (4a)	Platelet count ( $X 10^3$ /mm <sup>3</sup> ) within the control and hemofilter group.	105
Table (4b)	Comparison between platelet counts ( $X 10^3/mm^3$ ) in the control and hemofilter group.	105
Table (5a)	Prothrombin time (sec.) within the control and the hemofilter group.	107
Table (5b)	Comparison between prothrombin time (sec.) in the control and hemofilter group.	107
Table (6a)	Activated partial thromboplastin time (sec.) within the control and hemofilter group.	109
Table (6b)	Comparison between activated partial thromboplastin time in the control and hemofilter group.	109
Table (7a)	Fibrinogen concentration ( mg/dl ) within the control and hemofilter group.	111

Table (7b)	Comparison between fibrinogen concentration (mg/dl) in the control and hemofilter group.	111
Table (8)	Fibrinogen degradation products (μg/ml) within the control and hemofilter group.	113
Table (9a)	Antithrombin III (%) within the control and hemofilter group.	114
Table (9b)	Comparison between antithrombin III (%) in the control and hemofilter group.	114
Table (10a)	D-dimer concentration (ng/ml) within the control and hemofilter group.	116
Table (10b)	Comparison between D-dimer concentration (ng/ml) in the control and hemofilter group.	116
Table (11)	Comparison between the control and hemofilter group as regards blood loss (ml).	118
<b>Table (12)</b>	Comparison between both groups as regards ICU stay (day), ventilation time (hour) and hospital stay (day).	119

# List of Figures

Figure (1)	HS-accelerated inhibition by AT III on the surface of endothelial cells.	5
Figure (2)	TM- mediated PC activation by AT III, HCII, and PCI on the surface of endothelial cells.	7
Figure (3)	Inhibition of F Xa and TF-F VIIa by TFPI on the surface of endothelial cells.	10
Figure (4)	Platelet ultrastructure.	13
Figure (5)	Platelet function.	14
Figure (6)	Bi-directional trafficking across platelet surface	17
Figur (7)	Pathways of blood coagulation.	24
Figure (8)	Activation pathways of prothrombin.	32
Figure (9)	Structure of fibrinogen.	35
Figure (10)	Crosslinking of fibrin.	36
Figure (11)	Inflammatory response induced by CPB.	43
Figure (12)	Rolling, adhesion and aggregation of inflammatory cells on the vascular endothelium.	49

Figure (13)	Generation of thrombin activated via either the contact system or the extrinsic release of TF.	55
Figure (14)	Possible mechanisms of action of approtenin.	70
Figure (15)	Active site blocked F IXa .Effective replacement of F IXa.	71
Figure (16)	Ultrafiltration.	78
Figure (17)	Placement of ultrafiltration device within the extracorporial circuit.	78
Figure (18)	Comparison between hemoglobin concentration (mg/dl) in patients of control and hemofilter group.	102
Figure (19)	Comparison between hematocrit % in patients of control and hemofilter group.	104
Figure (20)	Comparison between platelet count (X10 <sup>3</sup> /mm <sup>3</sup> ) in patients of control and hemofilter group.	106
Figure (21)	Comparison between prothrombin time values (sec) in patients of control and hemofilter group.	108
Figure (22)	Comparison between activated partial thromboplastin time (sec) in patients of control and hemofilter group.	110
Figure (23)	Comparison between fibrinogen concentration (mg/dl) in patients of control and hemofilter group.	112
Figure (24)	Comparison between antithrombin III % in patients of control and hemofilter group.	115
Figure (25)	Comparison between D-dimer concentration (ng/ml) In patients of control and hemofilter group.	117

Figure (26)	Comparison between patients of control and hemofilter group as regards blood loss (ml).	118
Figure (27)	Comparison between patients of control and hemofilter group as regards ICU and hospital stay (day).	119
Figure (28)	Comparison between patients of control and hemofilter group as regards ventilation time (hour).	120

### List of Abbreviations

α<sub>2</sub>APα<sub>2</sub> AntiplasminAPCActivated protein C

**APTT** Activated partial thromboplastin time

AT III Antithrombin III
B-TG Beta thromboglobulin
CPB Cardiopulmonary bypass

**DSPG** Dermatan sulfate proteoglycans

EC Endothelial cells

FDA Food and Drug Association FDPs Fibrinogen degradation products

FFP Fresh frozen plasma
FPA &B Fibrinopeptide A & B
GAGs Glycosaminoglycans

GPs Glycoproteins
HB Hemoglobin
HC II Heparin cofactor
Hct Hematocrit

HMWK High molecular weight kininogen HSPG Heparan sulfate proteoglycans

ICU Intensive care unit

IL Interleuken

IR Ischaemic reperfusion
OCS Open canalicular system

PAI Plasminogen activator inhibitor

**PC** Protein C

PCI Protein C inhibitor
PCR Protein C receptor

**PDFG** Platelet derived growth factor

PF4 Platelet factor 4

PS Protein S

rPF<sub>4</sub> recombinant Platelet factor <sub>4</sub>

SCCS Surface connected canalicular system
TAT Thrombin antithrombin III complex

TF Tissue factor

**TFPI** Tissue factor pathway inhibitor

TM Thrombomodulin
TNF Tumour necrosis factor