Online ISSN: 2249-4618
Print ISSN: 0975-5888

Global Journal

of Medical Research: I

Surgeries and Cardiovascular System

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Highlights

Predictor of Acute Aortic

Study of Impact of Early Diagnosis

Discovering Thoughts, Inventing Future

VOLUME 15 ISSUE 2 VERSION 1.0

Global Journal of Medical Research: I
Surgeries and Cardiovascular System

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Volume 15 Issue 2 (Ver. 1.0)

Open Association of Research Society

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Contents of the Issue

Global Journal of Medical Research: I
Surgeries and Cardiovascular System
Volume 15 Issue 2 Version 1.0 Year 2015
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Aortic Wall Thickeness as a Predictor of Acute Aortic Dissection

By Jaroslav Benedik, Daniel Wendt, Fanar Mourad, Daniel Dohle, Lisa Himpel, Vivien Price, Konstantinos Tsagakis & Heinz Jakob

University Hospital Essen, Germany

Abstract- *Background:* Risk stratification for aortic dissection (AD) or rupture based on ascending aortic diameter and connective tissue disorders are inadequate. We have evaluated the impact of aortic wall thickness (AWT) on aortic wall quality.

Methods: Aortic wall cohesion of 496 patients divided into two groups according to AWT was analyzed using the Dissectometer, a device mimicking transverse shear stress. Correlation of cohesion testing (P7,P8,P9), histology as well as diameter of the ascending aorta with AWT were analyzed.

Results: AWT > 2.28mm was associated with decreased aortic cohesion (P7:131.7±66.3 vs.153.7±89.5 p=0.02; P8:2.95±1.55 vs.3.78±1,90 p<0.01; P9:4.22±1.75 vs.4.94±2.12 p<0.01) and increased media degeneration (45.8%vs.15.8% p<0.01) compared to AWT ≤ 2.28mm. Diameter of ascending aorta did not correlate with AWT (p=0.20). Majority of patients with AD presented with normal aortic diameter (13/18, 72.2%) and had an AWT > 2.28mm (15/18, 83.3%).

Keywords: *aortic wall, dissection, aortic wall cohesion testing.*

GJMR-I Classification: *NLMC Code: WG 265*

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Conclusions: Aortic wall thickness>2.28mm appears to correlate with decreased aortic cohesion as well as histological signs of aortic wall instability irrespective of aortic diameter.

Keywords: aortic wall, dissection, aortic wall cohesion testing.

I. Introduction

Acute aortic dissection (AD) is a serious disease with high morbidity and mortality, regularly presenting without any prognostic symptoms, but nevertheless being associated with underlying aortic wall pathology [1,2].

In addition to spontaneous dissection without triggering injury, acute aortic complications occur in approximately 0.16% - 0.35% of patients undergoing cardiac surgery as well as following other interventions involving aortic manipulation including intra-aortic balloon pump (IABP) insertion [3]. Currently, prediction of individual risk for future aortic dissection is mainly based on aortic diameter as well as history of connective tissue diseases (e.g. Marfan syndrome) or aortic valve abnormalities (e.g. bicuspid valve) [2]. Although it has been established that aneurysm size has a profound impact on risk of rupture, dissection and death, large studies have shown that a significant proportion of patients developing acute aortic dissection have a normal or only marginally enlarged aortic diameter [3]. Our current means of risk stratification for aortic dissection or rupture are therefore suboptimal, and prophylactic aortic replacement based solely on aortic diameter appears to be an insufficient strategy [4,5]. There is therefore a need to develop further diagnostic tools to predict the risk of future aortic complications. Aortic enlargement with resultant wall thinning was believed to be an important factor increasing wall stress and leading to aortic rupture or dissection. Therefore, it was the aim of this study to test the hypothesis that the aortic wall thickness (AWT) correlates to histological or clinical signs of aortic wall instability and cohesion as assessed by the Dissectometer device [6].

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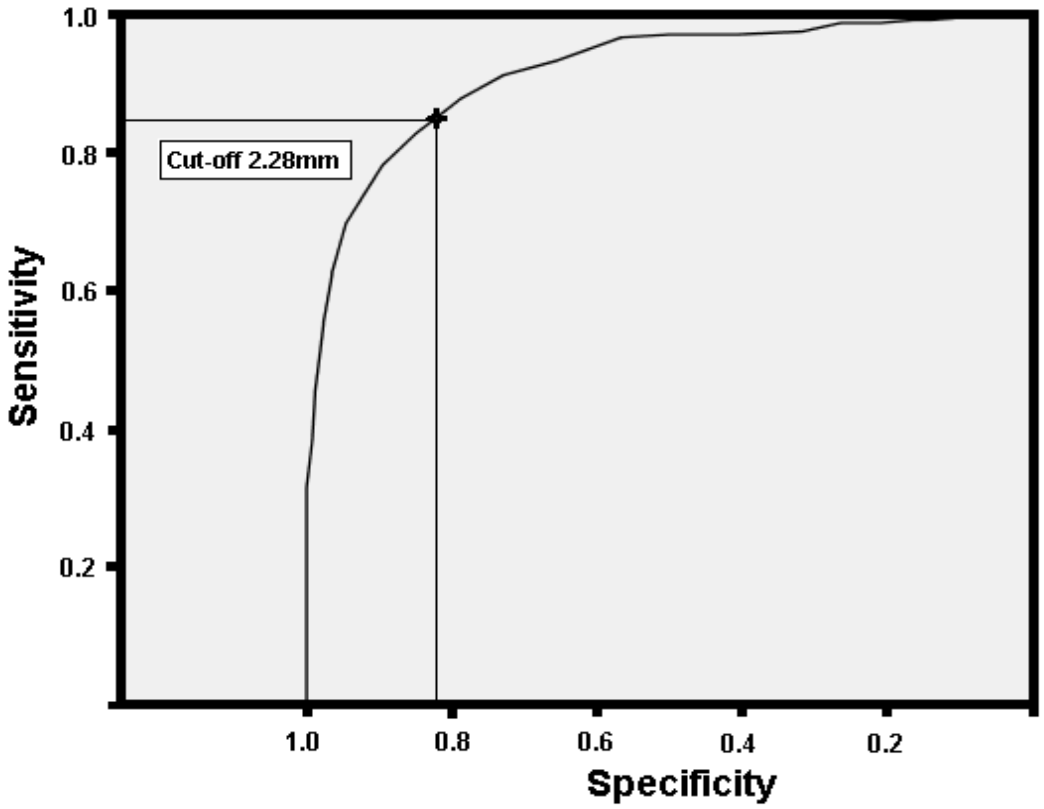
II. Materials and Methods

a) Study design

The study was approved by the Institutional Review Board and patients' written informed consent was obtained. This single-center, non-randomized study enrolled 496 consecutive patients undergoing surgery for aortic valve stenosis (AS) or regurgitation (AR), aortic aneurysms (AA) and coronary artery bypass grafting (CABG) (including concomitant procedures) at the West-German Heart Center Essen between March 2010 and December 2013. Patients with acute aortic dissection (ADD) were only included in this study if a piece of the aortic wall could be resected for histological and cohesion testing that was clearly unaffected by dissection.

The study population was divided into two groups according to aortic wall thickness: Group 1: AWT ≤ 2,28mm (n=260) and group 2: AWT > 2,28mm (n=236). The optimal cutoff level was defined by the largest sum of sensitivity and specificity of the AWT for histological signs of aortic wall instability using ROC analysis (Cut-off 2,28 mm: sensitivity 83% and specificity 85% see Fig. 1).

Figure 1



ROC curve - Sensitivity and specificity for cut-off 2.28mm

b) Sample collection

Surgery was carried out through a median sternotomy using cardiopulmonary bypass with ascending aortic cannulation. In patients with aortic valve disease or aortic aneurysm, a sample of the aortic wall was harvested from the edge of the aortic incision site (~ 3cm above the aortic valve), as previously described [6]. In patients undergoing isolated CABG, the sample of aortic wall was harvested using a rounded scalpel. The resulting hole was then used as the insertion point for a vein graft. In patients with acute type A dissection, only those patients in whom sufficient specimens of non-dissected aorta allowing for measurement of thickness and cohesion were included in the study.

The aortic sample was immediately placed in cold saline until the cohesion test was performed (within 2 hours of collection). Aortic wall thickness was measured immediately before cohesion testing using a micrometer (Kometex B.V./Hogetex, Netherlands).

c) Intraoperative echocardiography

TOE was performed with a multiplane 2.9–6.7 MHz (6T-RS) phased-array probe (Vivid i, GE Healthcare, Milwaukee, WI, USA) using a standardized protocol prior to cardiopulmonary bypass in all patients. The following aortic dimensions were measured: diameter of the aortic annulus, aortic sinuses, sinotubular junction and ascending aorta.

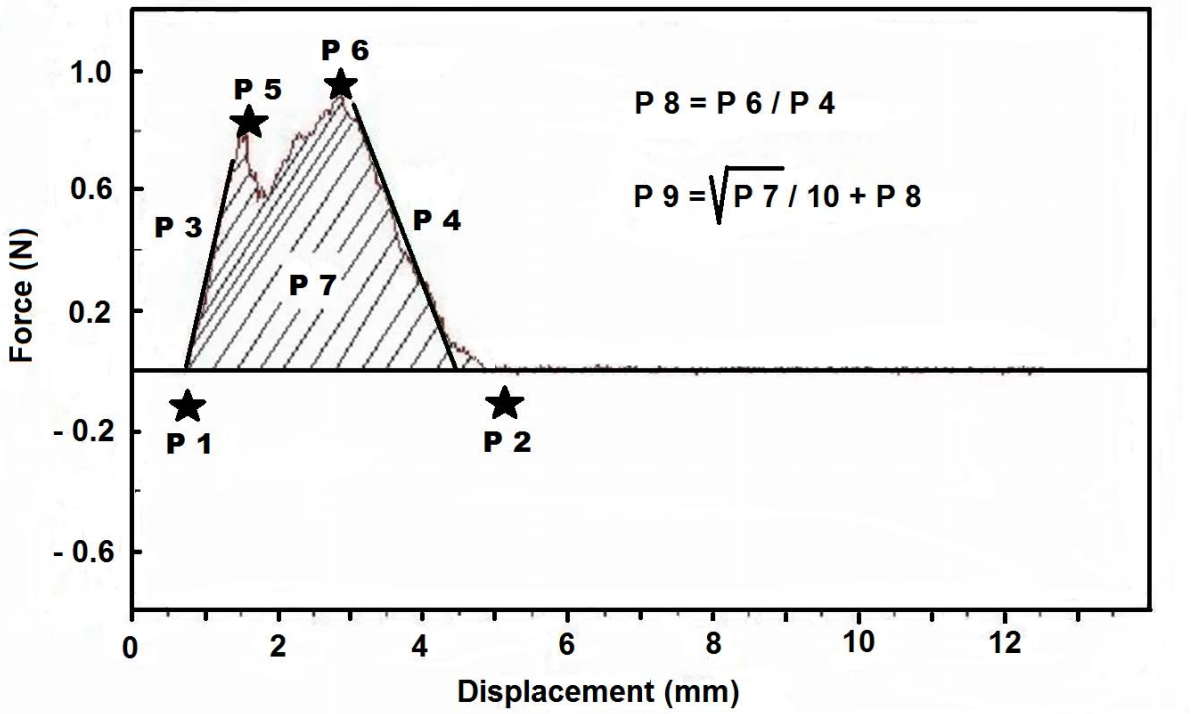
d) Aortic wall cohesion testing

Aortic wall cohesion testing was performed using the Dissectometer, a device mimicking transverse shear stress (simulating the acute dissection process), as previously described [6]. Results of the dissection were visualized as tensile strain curves (TSC), which were subsequently converted to numerical parameters.

P1, P2, P5 and P6 correspond to points on the curve. P1 (mm) is the beginning of the positive deviation – the point when the Dissectometer registers the tension in the sample. P2 (mm) is the point of the dissection and the power has a value of zero. P5 (N) is the first power maximum (at this point the power has decreased temporarily). After this point the aortic wall sample is damaged irreversibly. P6 (N) represents the "dissection limit" after which the power necessary to disrupt the aorta decreases. P3 ($N.mm^{-1}$) is the angle of the line between P1 and P5. This characteristic describes the elasticity of the aortic wall – the sharper the angle, the greater the elasticity of the aorta. P4 ($N.mm^{-1}$) is the angle of the power decrease, which characterizes the cohesion of the aortic wall. P7 (N.mm) represents the area under the TSC, which describes the total cohesion of the aorta. These seven parameters were used to mathematically derive the next two parameters, P8 and P9. P8 is described as the "dissection tendency" (calculated as the maximal force divided by the downward angle) and P9 as the "dissection potential"

(calculated as the sum of P8 and the square root of P7 divided by ten). The parameters with the highest sensitivity and specificity for discriminating between histologically stable and unstable aortic wall identified in a previous study (P7, P8 and P9) were analyzed in the present study (Fig. 2) [7]. One observer blinded to all patient data performed all cohesion tests.

Figure 2



Tensile strain curve – Localization of the parameters P1 - P7; mathematical formula for P8 and P9.

e) Histological examination

All samples were collected in 4% buffered Formalin, embedded in paraffin and cut to micrometer sections. These sections where stained with Hematoxilin and Eosin, and Elastica van Giessen. Histological examination was performed by an independent, blinded pathologist. The aortic wall was categorized using an integrated approach, by evaluating the media according to presence of vacuolization and texture disturbances as "pathological/media degeneration", or "intact /minimal changes". Media degeneration was defined as fibrosis of the media with fragmentation and/or loss of elastic fibers and increased deposition of proteoglycans. Media disruption was defined as disruption of elastic fibers in the media of the aorta.

f) Statistics

Descriptive statistics are summarized for categorical variables as frequencies (%). Pearson's χ^2 or Fisher´s exact tests were used for comparisons between groups. Continuous variables are reported as mean ± standard deviation and were compared using the Student´s *t*-test or Mann-Whitney U test. *P*-value of < 0.05 was considered to indicate statistical significance. All statistical analyses were performed using the SPSS System®, version 19.0 (IBM Corp., Armonk, NY, USA).

III. Results

Out of 496 patients, 260 had an ≤ AWT 2,28mm, while 236 patients presented with an AWT > 2,28mm. There were no difference in demographics and prevalence of comorbidities (age, gender, diabetes mellitus, chronic kidney insufficiency, hypercholesterolemia and chronic obstructive pulmonary disease) between the two groups (Table 1). Type of surgery and proportion of histology positive for aortic wall instability are summarized in table 2. A total of 109 patients underwent replacement of the aortic valve due to aortic stenosis (slightly more than in Group 2, $p = 0.07$). Coronary artery revascularization was performed in 285 patients ($p = 0.87$), in 134 cases as isolated procedure. 18 patients underwent surgery for aortic dissection (significantly more in Group 2, $p < 0.01$). While only 41 (15.8%) patients in Group 1 showed histological signs of aortic wall instability, the aortic wall of 108 (45.8%) patients in Group 2 was classified as histologically unstable ($p < 0.01$).

Table 1 : Demographics

n=496	Group1 (n=136)	Group 2 (n=360)	*P*-value*
Age (years)	65.0±12.9	65.8±12.7	0.69
Female	48 (35.3)	96 (26.7)	0.06
Hypertension	110 (80.9)	315 (87.5)	0.06
DM	28 (20.6)	66 (18.3)	0.57
Renal insufficiency	19 (14.0)	33 (9.2)	0.12
Hypercholesterolemia	67 (49.3)	190 (52.8)	0.49
COPD	14 (10.3)	37 (10.3)	1.00

*Data are presented as mean±SD or number (%); DM, Diabetes mellitus; COPD, Chronic obstructive pulmonary disease; *, group 1 versus group 2.*

Table 2 : Operation diagnoses and positive histology

n=496	Group 1 (n=136)	Group 2 (n=360)	OR	*P*-value*
AS	62 (45.6)	115 (31.9)	0.77	<0.01
AR	31 (22.8)	101 (28.1)	1.2	0.24
AA	23 (16.9)	87 (24.2)	1.3	0.08
CAD	74 (54.4)	211 (58.6)	1.0	0.40
Dissection	1 (0.7)	17 (4.7)	6.2	0.03
Positive Histology	24 (17.7)	161 (44.7)	2.1	<0.01

Data are presented as number (%); OR, Odds ratio; AS, aortic stenosis; AR, aortic regurgitation; AA, ascending aneurysm; CAD, Coronary artery disease;, group 1 versus group 2.*

Echocardiographic and Dissectometer-derived results are summarized in table 3, showing that aortic diameter as assessed by TOE (i.e. the annulus, aortic sinuses, sinotubular junction and ascending aorta) did not differ between the two groups. We observed statistically significant differences in aortic wall cohesion between the Group 1 and Group 2 as demonstrated by Dissectometer testing (P7: 153.7 ± 89.5 vs. 131.7 ± 66.3, $p < 0.02$; P8: 3.78 ± 1.90 vs. 2.95 ± 1.55, $p < 0.01$; P9: 4.94 ± 2.12 vs. 4.22 ± 1.75, $p < 0.01$), indicating a more stable aortic wall in patients with a thin aortic wall.

Table 3 : Transesophageal dimensions and TSC results

n=496	Group 1 (n=136)	Group 2 (n=360)	*P*-value*
Aortic annulus (mm)	24.5±2.2	24.5±2.4	0.74
Aortic Sinuses (mm)	33.5±6.3	34.4±7.7	0.62
Sino-tubular junction (mm)	30.8±7.2	31.5±8.2	0.70
Ascending aorta (mm)	35.1±9.0	37.0±10.2	0.09
P7	165.3±103.3	132.7±84.9	<0.01
P8	4.52±2.17	2.53±1.14	<0.01
P9	5.74±2.37	3.62±1.35	<0.01

A significant correlation (CC) was found between aortic wall thickness and the parameters P7 (CC 0.13; $p = 0.04$), P8 (CC 0.29; $p < 0.01$) and P9 (CC 0.27; $p < 0.01$) in cohesion testing, presence of acute dissection (CC 0.17; $p < 0.01$) and positive histological changes in aortic media (CC 0.55; $p < 0.01$). Diameter of ascending aorta did not correlate with AWT (CC 0.06 $p = 0.20$).

Of 18 patients presenting with acute type A aortic dissection, 13 (72.2%) had an aortic diameter of less than 45 mm and the majority of these patients presented with an AWT > 2,28 mm (15/18; 83.3%).

III. Discussion

Acute aortic dissection is a serious disease with significant associated morbidity and mortality, which often occurs spontaneously in individuals with no significant comorbidities, but is also observed as a rare complication of cardiac surgery as a result of aortic wall injury from cannulation, cross-clamping, aortic incisions

or central anastomoses of bypass grafts [3]. The mechanisms leading to high susceptibility for further injury and development of localized subadventitial hematoma or widespread acute dissection in some patients are only poorly understood. Luk et al [8] described histological changes including intimal thickening, cystic media necrosis and disruption of the media in excised aortic samples of patients undergoing surgery for AD as a post-operative complication after primary cardiac surgery. The majority of changes were located near the cannulation sites, aortic incisions or cross-clamping sites and near to stitch holes or knots. In addition, non-dissected samples of aortic wall still showed changes in vessel architecture. Williams et colleagues [3] published data from the Society of thoracic Surgeons (STS) database analyzing prevalence and risk factors for intraoperative AD in more than 2 million patients undergoing elective surgery. 1294 patients suffered from intraoperative AD (0.06%). Patients with intraoperative dissection were more likely to be older, female and have a history of previous cardiac surgery, compared to patients without intraoperative dissection.

Another retrospective single-center study including mainly patients undergoing CABG reported an incidence of 0.12% of intraoperative or early postoperative (8-32 days) AD [9]. In all cases of intraoperative AD, the primary tear was located at the cannulation site. Histological examination of the aortic wall revealed cystic media necrosis in four cases, atherosclerosis in three cases, but no pathological changes in two cases. Aortic diameter did not predict the development of AD.

Current guidelines suggest intervention in the general population when the thoracic aorta exceeds 5.5 cm in diameter, as the annual rupture risk outbalances the perioperative mortality. However, several large studies of patients with small aortic aneurysms have revealed heterogeneity in patterns of growth and rupture potential among patients with a moderate dilatation of the aorta. Indeed, the majority of patients with acute type A aortic dissection present with aortic diameters <5.5 cm and thus do not fall within current guidelines for elective ascending aortic replacement [3,10].

Besides aortic diameter, many other properties of the aorta and their potential roles in the pathogenesis of aortic dissection have been discussed. Beller et al [11] demonstrated that the most distinct motion of the ascending aorta can be observed approximately 2 cm above the STJ, which is the most frequent location of intimal tear formation in the process of AD, indicating a potential role for aortic dissection.

As previously mentioned the histological changes observed in patients with acute aortic dissection are heterogeneous and vary from minimal changes, to fragmentation of elastin or fibrosis to complete media necrosis. However, these changes are not specific as they have also been frequently observed in healthy patients [12].

Hypertension is widely believed to be a major triggering factor for the development of AD [13,14,15,16]. Sommer [17] showed that distension of the aorta during systole induces radial movement of the wall layers against each other relative to the distance from the aortic center, as reflected by the diameter of the aorta. Based on this mechanistic approach, increased systolic pressure produces greater expansion of the aortic wall and movement of aortic layers, and might be more harmful than diastolic pressure in conferring dissection risk. Movement of the radial layer caused by systolic pressure might cause a rupture between tunica adventitia and media making the aortic wall susceptible to further injury, leading to dissection. This mechanism could explain the higher dissection risk in those patients with a large aorta or systolic hypertension than patients with a normal aorta or diastolic hypertension.

Bicuspid aortic valve (BAV), the most common congenital heart defect, has long been implicated in the development of severe aortic complications. However, in our previous study comparing the cohesion of the aortic wall in patients presenting with bicuspid and tricuspid aortic valves, we did not detect any difference between these two groups [18]. One explanation for this discrepancy might be the higher prevalence of hypertension in the tricuspid group in this study, possibly modifying aortic wall cohesion of this patient cohort more distinctly.

Another potential factor in the pathogenesis of AD may be the impairment of vasa vasorum flow, as postulated by Angouras et al [19]. Impairment of blood supply to the thoracic aorta in an experimental setting leads to abnormal morphology of collagen and elastin resulting in increased stiffness of the aortic wall. When ischemia of the aortic wall results, even mild traction might cause separation of the aortic layers, with resultant aortic dissection.

Currently, there are only limited data available on the impact of aortic wall thickness on the development of aortic dissection. Fanari et al [20] demonstrated that combined intimal/medial thickness as well as total aortic wall thickness was greater in patients with AD compared to controls. For this reason, the current study focuses on aortic wall thickness, a parameter which can be easily measured preoperatively in routine practice using TOE or CT. We were able to show that aortic wall thickness > 2mm predicts histological pathology, and poorer aortic wall cohesion as measured by Dissectometer. This finding is underlined by the clinical fact that incidence of acute dissection was significantly higher in patients with a thicker aortic wall. At first glance, this seems to be

paradox as aortic enlargement with consecutive wall thinning are believed to be the most important factors increasing wall stress and leading to aortic rupture or dissection.

IV. Conclusion

The current study could showed that patients with AWT of more than 2,28 mm may be at higher risk of aortic wall instability, as measured by Dissectometer examination and histology compared to patients with a thinner aortic wall. However, a larger prospective study with a long-term follow-up is necessary to confirm our findings.

Limitations

There are some limitations of our study. Firstly, our study suffers from the general limitations of a single-center, retrospective investigation. A larger prospective study with a long-term follow-up is necessary to confirm our findings. Although histology is considered to be the standard technique for analyzing aortic wall stability, the predictive value of this method is unknown.

V. Acknowledgments

The present study was presented at the 28th annual meeting of the European Association for Cardiothoracic Surgery, October 11-15, 2014, Milan, Italy.

Funding Sources

This research received no grant from any funding agency in the public, commercial or not-for-profit sectors.

Disclosures

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agreed to the manuscript as written. The authors disclose no conflict of interests in regard to the present manuscript.

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Global Journal of Medical Research: I
Surgeries and Cardiovascular System
Volume 15 Issue 2 Version 1.0 Year 2015
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

A Study of Impact of Early Diagnosis in the Management of Choledochal Cysts of Infancy and Childhood – Experience and Analysis of 205 Cases

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Abstract- *Introduction:* Choledochal cyst not an uncommon encountered pediatric surgical practices. Advances in technology have impacted timing of diagnosis. Advances in instrumentation and surgical access have added yet another way of excion. But the exact impact of early diagnosis on surgery of choledochal cysts have not been analysed and reported. Hence this attempt to analyse the three periods of choledochal cyst, namely 1. PTC (Percutaneous Trans-hepatic Cholangiography) and ERCP (Endoscopic Retrograde Cholangio – pancreatography), 2. USG (Ultrasonography) and CT Scan (Computerised Tomography era, and 3 .Period of MRCP (Magnetic Resonnace Cholangio –Pancreatico-graphy) with reagrds to impact of early diagnosis in the management of Choledochal cysts.

Materials and Methods: A total of 205 cases of choledochal cysts treated by the team were analysed. The data retrieval was from aaself developed Microsoft Access based soft ware used by senior pediatric surgeon.

Keywords: *choledochal cyst, roux en y hepaticodochojejunostomy, anomalous pancreatico biliary portal junction, long channel.*

GJMR-I Classification: *NLMC Code: WI 100*

Strictly as per the compliance and regulations of:

A Study of Impact of Early Diagnosis in the Management of Choledochal Cysts of Infancy and Childhood – Experience and Analysis of 205 Cases

Dr. G Raghavendra Prasad [α], Dr. Kasha Aishwarya [σ] & Dr. J V Subbarao [ρ]

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Materials and Methods: A total of 205 cases of choledochal cysts treated by the team were analysed. The data retrieval was from aaself developed Microsoft Access based soft ware used by senior pediatric surgeon. The parameter studied was actual impact on surgical aspects of the three main components of surgery of choledochal cysts, namely 1. Approach to cyst excision per se, 2. Management of distal end, 3. Restoration biliary drainage.

Results: The advances in imageology have lead to early diagnosis and early surgery before complications develop. This has impacted in disappearance of delayed presentation with complications as seen by the number of cases diagnosed in neonatal period. Neonatal, perinatal, rarely antenatal detection of choledochal cysts was possible due to advances in imaging choledochal cysts. All children underwent excision of cyst and common hepaticodochojejunostomy. The safety of excision particularly when dealing inflamed, adherent choledochal cysts was better with open conventional excision. Similarly the confidence of handling the distal end was more with open surgery. Laparoscopy and Robot assisted have added another surgical access to choledochal cysts. Minimal access and magnification added to better visual appreciation, but ergonomics, cost, and availability, approach to distal end remain still to be validated.

Conclusions: The present series clearly show the increase in the incidence of Choledochal cyst due to advances in imageology. Also has impacted early diagnosis is early surgical removal and there by delayed presentation , and with complications like stone, recurrent cholangitis, pancreatitis, biliary cirrhosis This technological anatomical detailing has not reflected any significant change in the surgical management of Choledochal cyst. The advances in instrumentation and minimal access surgery and Robot assisted surgery still needs to validated as safe and can be used as standard surgical option for excision of choldochal cyst.

Keywords: *choledochal cyst, roux en y hepaticodochojejunostomy, anomalous pancreatico biliary portal junction, long channel.*

I. Introduction

Choledochal cyst is cystic dilatation of extra and/or intra hepatic biliary dilatation. Choledocal cyst is not uncommon particularly after the invention of high resolution USG and now MRCP. They continue to perplex surgeons regarding etiology particularly anomalous Pancreatico- biliary ductal junctions. Purpose to question if any advances in diagnosis changed the management of Choledochal Cyst.

II. Aims and Objectives

PTC: Percutaneous trans hepatic cholangiogram

ERCP: Endoscopic retrograde cholangiogram

C T Sca : Computerized tomogram

To present experience of 205 cases of Choledocal cyst across 1980's, an era of P.T.C - ERCP. 1990"s, an era of USG-CT scan and late part of 1990's & 2000 era dominated by MRCP difficulties in diagnosis in USG- era and accurate anatomical delineation in MRCP era targeted yet in this presentation.

III. Materials and Method

A total 205 cases were seen and treated from 1983 till 2014. This period is divided this period is divided in 3 periods.

Period 1: from 1983 - 1990 i.e, period of P.T.C and ERCP n=21

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Period 2: from 1991 -1998 i.e, period of USG and CT scan n=38

Period 3: from 1992 – 2014 i.e, period of MRCP dominance n=146

A particular emphasis during analysis was made to know if USG and MRCP have influenced the diagnosis and treatment of choledochal cyst, particularly three components in management of Cyst per se, distal end and Biliary drainage were parameters of study.

Period 1 had 21 cases, period 2 had 38 cases, period 3 had 146 cases, age of presentation, clinical presentation, type of Choledocal cyst, surgical treatment offered and outcome was analyzed.

IV. Results

Table 1: shows the number of cases in each period. Period 1 had 21 cases, period 2 had 38 cases, period 3 had 146 cases.

Table 1 : Case distribution in relation to period of study

Year	Number of cases	%
1983 - 1990	21	10.2%
1991 - 1998	38	18.5%
1999-2014	146	71.2%

It is obvious from table 2 during the era of P.T.C and ERCP, most were diagnosed between 5-15 years, only 3 out of 21 cases (1.5%) were diagnosed in 1- 5 years, none were diagnosed below 1 year of age. Period 2 shows 19 out of 38 cases (9.3%) were diagnosed during infancy. In period 3, Antenatal diagnosis was made in 8 cases (3.9%) and 103 out of 146 cases (50.2%) during these period were diagnosed and treated before 5 years of age.

Table 2 : Distribution according to age at diagnosis.

Year	O/ month	%	<1 year	%	1-5 years	%	5-10 years	%	10-18 years	%
1983-1990	0	0	0	0	03	1.5%	07	3.4%	11	5.4%
1991-1998	0	0	08	3.9%	11	5.4%	15	7.3%	04	1.9%
1999-2014	08	3.9%	37	18%	58	28.3%	21	10.2%	22	10.7%
Total	08	3.9%	45	21.9%	72	35.2%	43	20.9%	37	18%

Pain abdomen was seen in majority of cases, while jaundice was seen less frequently. Palpable mass seen in only 5 patients in the series. 3 patients were presented with acute pancreatitis picked up on USG and MRCP. 12 babies presented with biliary peritonitis. 72 were picked up incidentally from an USG-abdomen. For other symptoms see table 3 in all the three eras. Type I out of 4 was commonest Choledochal cyst seen. Type 2 choledochal cyst was seen in four children. Type 3 choledochal cyst was seen in one child. No Caroli's disease was seen in this series.

Table 3 : Clinical presentation in relation to period of study

Clinical presentation	Period 1	Period 2	Period 3
Jaundice	02(0.9%)	04(1.9%)	08(3.9%)
Pain abdomen	18(8.8%)	22(10.7%)	54(26.3%)
Mass	01(0.5%)	0	04(1.9%)
Acute appendicitis	0	0	06(2.9%)
Acute peritonitis	0	04(1.9%)	08(3.9%)
Incidental	0	08(3.9%)	66(32.2%)

All the children underwent excision of the cyst and hepatico-jujenostomy, Lilly's technique used in 5, 1 child in type 2 diverticulum had diverticulectomy + repair of CBD. 1 child born with biliary peritonitis died, remaining patients were alive. Follow up ranged from 1 year to 25 years.

Complete excision of the cyst, complete excision of distal end without damaging pancreatic duct and at least 25 cms of Roux en Y hepaticodochojejunostomy were the end points of surgery. Choledochoscopy of distal end was done using cystoscope in two but later not felt to have added any extra information.

Table 4 : Frequency of type of Choledochal cyst in relation to period of study.

Type of Choledochal cyst	Period 1	Period 2	Period 3
Type 1/4	21(10.2%)	38(18.5%)	141(68.8%)
Type 2	0	0	04(1.9%)
Type 3	0	0	01(0.5%)

V. Discussion

Choledochal cyst is a rare disease of the biliary tract in children. There are five main types of Choledochal cyst described by TODANI et al., [(I)] The estimated incidence in western countries varies between 1 in 100000 and 1 in 150000. The incidence is higher in Asia and occurs more in women with a male to female ratio of 1: 3 to 1: 4.[(2)] In our series of study of 205 cases 168 cases were of age group of less than 10 years.

The etiology of Choledochal cyst still remains unclear. One of the most accepted hypothesis is proposed by Bobbit et al..<3) is the presence of an anomalous Pancreatico- Biliary ductal confluence proximal to the regulatory control of sphincter mechanism within the duodenal wall. This predisposes reflux of pancreatic enzymes with deconiugated bile. This induces chronic inflammation predisposing dilation of the biliary tree wall. [(3, 4)] Although Anomalous Pancreatico Biliary Portal Junction is not that frequently reported in other series. The present series also had only 15 cases with long common channel.

The clinical triad of jaundice, mass and pain is considered as the most common and significant findings in the diagnosis of the Choledocal cyst. Surprisingly no patient showed this triad in our series. We found pain abdomen 45.8% as the most common presenting finding of Choledochal cyst as described in a study by Bukukyavuz et al.[(5)]

Rajeev Dhupar et al., [(6)] reported 26% cases presented without any symptoms. But, rather as an incidental finding at CT Scan, Cholangigram or at laparoscopic surgery for other reasons. Our studies noted 36.1% of cases as an incidental diagnosis most of them being in period 3. The incidental finding of Choledochal cyst is on rise due to advanced diagnostic techniques.

Diagnosis of Choledochal cyst was made by different techniques in different periods of study as per the most reliable diagnostic tool of that time including x-ray, PTC, ERCP, USG, CT Scan and ERCP.

The PTC and ERCP were definitive test with 80-90% diagnostic accuracy. The advantage of this is they delineate the anatomy of biliary tree. As both of them are invasive procedures they were associated with complications. It was considered that intra- op PTC as mandatory for knowing anatomy during this period.[(7, 8)] The present series PTC – ERCP era 18/21 underwent PTC.

Anwaza et al., first used USG for the diagnosis of Choledochal cyst when it is small. USG Is the first non-invasive imaging modality of choice in evaluation of patients suspected to have bile duct dilatation.[(9)] In a study by J.S. devries et al., USG has been 93% diagnostic as primary imaging. But, for surgical procedure of Choledochal cyst the detailed anatomy made possible only by aid of improved diagnostic techniques like CT & MRCP, CT Scan can clearly visualize the location and relationship with surrounding structures. [(9,10)] USG has picked up one incidental Choledochal cyst. In the present series too larger number of choledocal cysts were diagnosed and treated in USG and MRCP era.

Past decade has seen MRCP replaced all other investigations as it is non- invasive and gives clear cut anatomy of biliary tree for good surgical plan.[11] Antenatal diagnosis by Antenatal high resolution ultrasound & fetal MR have reported Choledochal cyst with Biliary Atresia. [(12).]

The present serieaparticlualrystress that advances in imaging have lead to early diagnosis AND THRE BY decreasing late diagnosis , presentation with complications like stones, pancreatitis, recurrent cholangitis , biliary cirrhosis Choledochal cyst should be treated by Surgery as it is highly associated with the risk of malignancy(17) spontaneous or traumatic rupture have been reported by Suneel Chauhan et al.,

In our series out of 205 cases studied 204 presented with type 1 /4 & type 2, all of them underwent complete excision of cyst with Roux-en-y jejunostomy as treatment of choice as proposed by Kasai et al., and shown good results. One case presented with type 3 and underwent excision with repair as treatment of choice. All the patients who underwent excision and repair and are alive but, one expired due to biliary sepsis / peritonitis and associated complications

Despite the advances in accurate anatomical delineation by advanced technology of imaging the surgical approach to the three main components of operation namely Choledochal cyst per se, distal end & biliary enteric anastomosis remains the goals of treatment. As of now open Choledochal cyst excision in toto, complete excision of distal end not injuring pancreatic duct Roux en Y common Hepaticodocho Jejunostomy is the standard care. . Laproscopic Choledochal cystectomy [(14)] and Robotic assisted Choledochal cyst excision [(15)] is being tried elsewhere. Although advances in surgical instrumentation, endo surgery and Robot assisted are gathering momentum for regular use, still they cannot be termed as standard care. The cyst excision itself cannot be as safely addressed in laroscopiic or Robot assisted, particularly

in the presence of repeated infections. Portal vein is surely safer in open choledochocystectomy as compared to Laparoscopic or Robot assisted excision. Laparoscopic or Robot assisted excsiuon related accidental injury to portal vein makes immediate laparotomy more time consuming and cumbersome , with consequences of blood loss and biliary injuries in attempting hemostasis.

The time taken and not so effective and adequate addressing of the distal end continue to be not accepted by purists. Addressing Distal end by a magnified view of laparoscope, although is an advantage, still what is practiced and is shown in many surgical workshops by experienced endosurgeonsis convenient ligation rather than complete distal end excision. This may be due to the apprehension of injuring pancreas and or duodenum. The open conventional approach particularly aided by an operating loop, one can safely and surely deal exactly the distal end.

Common Hepaticodochoduodenostomy[16] although claims as effective as Roux en Y Common Hepaticodocho Jejunostomy, long term results of Common Hepaticodocho duodenostomy are still awaited to be accepted as a part of standard care of Choledochal cyst excision. As of now open Choledochal cyst excision with complete excision of distal end and atleast 25cms of Roux en Y Common Hepaticodocho Jejunostomy seems to be the gold standard. Laparoscopic & Robotic approach to inflamed, adherent Choledochal cyst may not be acceptabl and safe e[15,16]

VI. Conclusion

The present series clearly show the increase in the incidence of Choledochal cyst due to advances in imageology. Also has impacted early diagnosis is early surgical removal and there by delayed presentation , and with complications like stone, recurrent cholangitis, pancreatitis, biliary cirrhosis This technological anatomical detaining has not reflected any significant change in the surgical management of Choledochal cyst. The advances in instrumentation and minimal access surgery and Robot assisted surgery still needs to validated as safe and can be used as standard surgical option for excision of choldochal cyst.

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Global Journal of Medical Research: I
Surgeries and Cardiovascular System
Volume 15 Issue 2 Version 1.0 Year 2015
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Coronary Artery Disease and Pregnancy

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Abstract- The current classification and protocols that are followed in the Heart Disease and Pregnancy National Center (SNCE abbreviation for Servicio Nacional de Cardiopatía y Embarazo, in Spanish); regarding coronary artery disease associated to pregnancy are presented. Concise guiding principles concerning the diagnosis, evaluation, and management of coronary artery disease during pregnancy, labor, and postpartum period are offered.

Keywords: *coronary artery disease, acute coronary syndromes, pregnancy.*

GJMR-I Classification: *NLMC Code: WG 113*

Strictly as per the compliance and regulations of:

Coronary Artery Disease and Pregnancy

Jesús Ernesto Pérez Torga [α], Dr. Pedro Antonio Román Rubio [σ], Iraimis García Sánchez [ρ] & Iraimis García Sánchez [ω]

Abstract- **The current classification and protocols that are followed in the Heart Disease and Pregnancy National Center (SNCE abbreviation for Servicio Nacional de Cardiopatía y Embarazo, in Spanish); regarding coronary artery disease associated to pregnancy are presented. Concise guiding principles concerning the diagnosis, evaluation, and management of coronary artery disease during pregnancy, labor, and postpartum period are offered.**

Keywords: coronary artery disease, acute coronary syndromes, pregnancy.

I. Introduction.

Although coronary artery disease (CAD) is not frequent in pregnancy, its incidence is rising (approximately 6.2 cases per 100 000 pregnancies in USA), as a consequence of planning reproduction at ages higher than 35, the presence of coronary risk factor such as hypertension, preeclampsia, diabetes, smoking, and the use of assisted reproduction techniques.[1-3] The SNCE set the CAD related to pregnancy in three different clinical context: 1) known CAD in a patient planning getting pregnant, 2) known, stable or unstable CAD, in the already pregnant woman o parturient, and 3) CAD debuting during pregnancy, labor or puerperium –usually as acute coronary syndrome-.

II. Diagnosis and Assessment of CAD Associated to Pregnancy

Diagnosis of CAD is principally based on the history, confirmed by some laboratory investigations. The clinical presentation is similar to non-pregnant patients, with some features that should be kept in mind.[4,5] As pregnancy advances a reduction in functional capacity is normal. Most patients in the third trimester are in New York Heart Associations (NYHA) functional class II.[1,5] Pregnancy itself predisposes to myocardial ischemia, due to increased cardiac output, heart rate, and heart dimensions; in the other hand, myocardial oxygen supply could be compromised by a reduction in hematocrit, diastolic blood pressure, and subsequence coronary driving pressure. Pregnancy, as well as puerperium, increases the likelihood of thrombosis, as a consequence of higher serum levels of fibrinogen, coagulations factors, and enhanced platelet aggregation. The fibrinolytic activity is also reduced. Pregnancy increases the risk of myocardial infarction in four o five thresholds, compared with non-pregnant women.[1,2,6]

Some patients might confuse symptoms corresponding to CAD with discomfort caused by pregnancy. An episode of thoracic pain, with typical location and radiation, require excluding CAD. When chest pain is atypical or occurs in particular settings –e.g. immediately after a cesarean delivery-, a high grade of suspicion is necessary for making diagnosis.

The *Electrocardiogram* (EKG) in pregnant women shows several variations considered to be normal ones, such as, left QRS axis deviation, atrial and ventricular ectopic beats, sinus tachycardia, T wave inversion, ST segment depression without a rise in serum markers of cardiac damage. New Q waves in DIII, and less frequent in aVF have been described.[1,2,6,7] That is why, the combination of clinical data, serum markers of cardiac damage, and cardiac image (echocardiography) is recommended for a correct diagnosis. For identifying acute coronary syndrome the use of cardiac Troponins is mandatory, because serum levels of Creatine Kinase and its MB fraction are elevated because of the gravid uterus and placenta.[1,2,5] The *Holter Monitoring* could be useful in some cases, without any risk. In selected patients, with a high suspicion of CAD, the *Exercise Testing* might be helpful, using stationary bicycle ergometer or treadmill submaximal protocols –first modality is preferred-, with a 70 - 80% of predicted maximum heart rate as goal. The use of echocardiography improves the sensitivity and specificity of the test, and it is secure.[1,2]

The assessment of *Myocardial Perfusion with Radionuclide Imaging* is proscribed. *Dobutamine Stress Echocardiography* should also be avoided. *Coronary Computed Tomography Angiography,* where high doses of radiation are delivered to mother and fetus, is not recommended unless absolutely necessary.[2] When coronary anatomy evaluation is needed, the use of *Invasive Coronary Angiography* is preferred. The maternal radiation exposure should be kept in mind; though the procedure represents a 7 mGy maternal exposure dose, only 20 - 30% corresponds to fetal exposure (1,5 mGy), which is far enough of the estimated "secure" radiation exposure dose in pregnancy of 50 mGy (5 rad).[2,5,6,8,9] Radiation exposure to the fetus can be minimized by lead shielding of the

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mother's abdomen and pelvis, and –if possible- abstain to irradiates pelvis and abdomen during catheter advance to thoracic aorta. Radial arterial access is preferred. Contrast ventriculography is not recommended since ventricular function can be appropriately assessed with other methods.[2,8,9] The procedure should be performed in centers with extensive experience, and if it is undertaken after 26 weeks of pregnancy, obstetric and neonatology standby should be available in case of premature labor.

III. MAnagement of cad during Pregnancy, Labor, and Puerperium

The available information about the management of heart disease during pregnancy is based on case reports, case series, or retrospective analysis of large series, and sometimes, expert opinions. Prospective randomized trials, and the experimentation with new drugs or procedures during pregnancy or lactation is forbidden for ethical reasons, so pharmaceutical companies usually caution about the use of their products in pregnant women. That is why; recommendations are nearly all wide-ranging, and based on accumulated experience. Many of these strategies are current practice in SNCE.

1. *Known CAD in a patient planning getting pregnant:* women of reproductive ages with known CAD should be included in the Preconception Risk Program of Primary Health Care Setting (PHCS). Pregnancy is feasible when the patient is free of symptoms. Referral from PHCS to a cardiovascular specialist is mandatory, and the information flow bidirectional. Exercise testing before pregnancy might identify whether the patient will tolerate the hemodynamic changes of pregnancy, labor, and puerperium.[1,2] Those women with NYHA functional class II o more before pregnancy could not be capable to tolerate it, with worsening of symptoms as pregnancy progress.[1,2,6,8] When the patient decides to get pregnant angiotensin-converting enzyme (ACE) inhibitor therapy, angiotensin receptor blocker (ARB), direct renin inhibitor Aliskiren, and statins should be withdraw. Aldosterone antagonists such as eplerenone and spironolactone should also be avoided.[2] Beta blockers are safe, and cardioselective agents are better. Atenolol (FDA D category) should be avoided unless necessary; metoprolol and propranolol (noncardioselective) are preferred.[1,2] Oral nitrates are considered to be safe. Calcium channel blockers (CCB) are relatively safe too. The most employed in pregnancy has been nifedipine in the treatment of hypertension. If CAD is diagnosed the sustained-release preparations are the best choice. Verapamil and diltiazem are most used for their negative chronotropic effect (both FDA C category), but diltiazem is seldom used in SNCE for some report of fetal malformation.[1,2,4,6] Low dose of aspirin is safe. There is less information regarding clopidogrel, but recent reports indicate that the administration during pregnancy is secure.[1,2,10,11] If the patient is receiving dual antiplatelet therapy for intracoronary stent, it is reasonable to delay pregnancy until one year after stenting, then clopidogrel could be withdraw and continue with aspirin alone. If previous myocardial infarction has occurred, getting pregnant should be wait until the patients is free of symptoms –NYHA class I-, there is not an ischemic systolic dysfunction of the left ventricle –left ventricle ejection fraction less than 0.50-, inducible ischemia, nor electrical or hemodynamic instability.[1,2,5,6,8]

2. *Known, stable or unstable CAD, in the already pregnant woman o parturient:* patient care in this category should be multidisciplinary, including obstetricians, cardiologists, and anesthetists in first place, and also psychologists, genetics professionals, and others. In the first contact with the SNCE the patient undergoes to risk assessment for mother and fetus, and also counseling. The presence of symptoms, functional class, left ventricle dysfunction, arrhythmias, inducible ischemia, and other feature, are considered. The majority of recommendations commented before concerning cardiovascular drugs remains. Anemia in the pregnant ischemic woman should be promptly treated. If there are no symptoms, or they are mild, pregnancy should advance until spontaneously ends. If frequent symptoms or further complications are suspected as pregnancy progresses, patient should be given corticosteroids for fetal lung maturity. In these cases pregnancy conclusion might be counseled. Obstetric team will pay special attention to fetal well-being, observing any influence of cardiovascular drugs on fetal growth, heart rate, amniotic fluids, and uterine perfusion. Vaginal and spontaneous delivery is better in stable CAD patients.[1,2,6,8] Pain, anxiety, and adrenergic stimulation during labor could be risky, so; it is recommended to maintain anti-ischemic therapy, epidural analgesia, and obstetrical procedures to shorten the total duration of labor, particularly the second stage, if needed. Obstetric team should keep a low threshold for cesarean surgery if labor prolongs or patient deteriorates.[2] Unstable patients (NYHA class III-IV) should undergo to urgent cesarean delivery.[6,8] Cesarean surgery when using anti-platelet therapy increases the risk of bleeding. In some cases, our team has decided to interrupt the use of anti-platelet (aspirin and clopidogrel), and began administration of peripartum heparins protocols. Excessive bleeding

should be avoided, and treated promptly. The use of prolonged tocolysis with adrenergic agents could be dangerous. Postpartum ergot derivates are proscribed. Use of selective 5-hydroxytryptamine agonists for migraine headache has been associated to coronary vasoconstriction. Neonatologist should be told about mother´s ante partum beta blocker consumption, because several complications in newborn are likely (e.g. apnea, bradycardia, hypoglycemia, prolonged jaundice).[1,2] The multidisciplinary team should operate resting on an appropriated infrastructure, and if any complications occurs, provide immediate high quality care, including treatment for acute coronary syndrome, with cardiac catheterization laboratory access, ICU, operating room for cesarean, newborn intensive care units; and facilitated communications and motion of all parts.

3. *CAD debuting during pregnancy, labor or puerperium (acute coronary syndrome):* the largest part of available data regarding acute coronary syndrome (ACS) during pregnancy correspond to ACS with ST segment elevation (ACS-STE), with a related maternal mortality that ranges from of 5.7 to 37%.[1] Usually mortality rate is about 10%, as well as fetal mortality. Most of fetal deaths are consequence of maternal loss.[4] In almost half of ACS during pregnancy, the typical etiology of thrombotic occlusion due to atherosclerotic plaque rupture is not present.[4,10,11] Thus, reperfusion strategies using thrombolytic agents would be ineffective in a lot of cases. Based on maternal age, presence of coronary risk factors, moment of occurrence (antepartum, peripartum, or postpartum) the possible etiology might be suspected, but only coronary angiography would provide certainty. In patients with coronary risk factors, few weeks of gestation, and 35 years old, or more, is very likely the presence of thrombus with unstable plaque, but also has been described thrombus without atherosclerotic plaque, coronary vasospasm, and even normal coronary arteries.[4,10,11] In peripartum and postpartum, coronary artery dissection is most frequently seen, affecting in 80% of cases de left anterior descending coronary artery. In this period vasospasm, embolus, and thrombosis has also been reported.[4]

In case of ACS during pregnancy, labor, or puerperium, the standard procedures for management of ACS should be followed,[1,2,4,6,8,11] admitting the mother in ICU, and her life been priority at that moment. Obstetricians should be consulted about the exact weeks of gestation and fetal viability. Diagnostic criteria for ACS-STE remain the same for non-pregnant women. Ideally all patients should undergo to urgent coronary angiography for diagnosis of specific etiology. Whenever not possible, the reperfusion strategy is selected for the physician analyzing risks and benefits of thrombolytics. Pregnancy is a *relative* contraindication for thrombolytics use. It is the authors' opinion that, in case of hemodynamic and electrical stability, inferior myocardial infarction, and a setting where coronary dissection o spasm is likely –young women, no coronary risk factors, peripartum or postpartum-, does not initiate a fibrinolytic therapy. When anterior myocardial infarction is diagnosed with hemodynamic comprise, lethal arrhythmias, women 35 years of age, or more, presence of coronary risk factors, antepartum period, and other situations indicating the probability of plaque rupture and thrombosis; then, use of fibrinolytic therapy should de considered. Thrombolytic agents practically do not cross placental barrier,[2,4] but are associated with placental micro hemorrhage and hematomas; this is the mechanism implicated if fetal damage. After cesarean delivery, and one week after vaginal delivery, fibrinolytic therapy is absolutely contraindicated.[2,12,13]

Cardiovascular medications commented before are also useful in ACS. Same precautions remain. The use of unfractionated heparin and low-molecular-weight heparins is secure.[2,4] In this circumstance, clopidogrel is indicated as usual, in combination with aspirin. For pain relief morphine remains the drug of choice, and it is safe during pregnancy. Its administration near delivery is associated with respiratory depression in neonates.[2,4,6,8,10,12] Glycoprotein IIb/IIIa receptor antagonists have not been evaluated in pregnancy, in high-risk acute coronary syndromes undergoing scheduled percutaneous coronary intervention (PCI), the physician might consider use them after detailed discussion with the patient regarding the risks and benefits.[1,2,4] It is important to favor the use or radial access, and bare-metal stents. Drug-eluting stents (DES) have not been investigated. The use of DES requires dual anti-platelet therapy for six months to a year, depending of kind used, so the risk of bleeding increases in case of progression of pregnancy, and further vaginal or cesarean delivery.[2,4,6,8] In unstable angina/non–ST-segment elevation myocardial infarction, a conservative strategy is better, reserving the invasive approach for high-risk patients. All previous comments concerning medications remain the same.

It is very important a multidisciplinary approach to pregnant patient with cardiovascular disease. Centers with greater experience and expertise are better. After an ACS recovery, the evaluation of etiology and consequences of the event is significant. Referral to genetic specialist, rheumatologist, hematologist, and other, depending on each case, is useful for identifying vasculitis, antiphospholipid syndrome, thrombophilia, and other possible no atherosclerotic causes of ACS. Differential diagnosis of ACS in pregnancy include preeclampsia, pulmonary embolism, amniotic

embolism, aortic dissection, and hypovolemic shock.[2,4,5,11]

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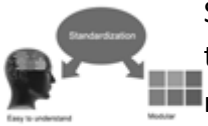

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Manuscript submission is a systematic procedure and little preparation is required beyond having all parts of your manuscript in a given format and a computer with an Internet connection and a Web browser. Full help and instructions are provided on-screen. As an author, you will be prompted for login and manuscript details as Field of Paper and then to upload your manuscript file(s) according to the instructions.

To avoid postal delays, all transaction is preferred by e-mail. A finished manuscript submission is confirmed by e-mail immediately and your paper enters the editorial process with no postal delays. When a conclusion is made about the publication of your paper by our Editorial Board, revisions can be submitted online with the same procedure, with an occasion to view and respond to all comments.

Complete support for both authors and co-author is provided.

4. MANUSCRIPT'S CATEGORY

Based on potential and nature, the manuscript can be categorized under the following heads:

Original research paper: Such papers are reports of high-level significant original research work.

Review papers: These are concise, significant but helpful and decisive topics for young researchers.

Research articles: These are handled with small investigation and applications

Research letters: The letters are small and concise comments on previously published matters.

5.STRUCTURE AND FORMAT OF MANUSCRIPT

The recommended size of original research paper is less than seven thousand words, review papers fewer than seven thousands words also.Preparation of research paper or how to write research paper, are major hurdle, while writing manuscript. The research articles and research letters should be fewer than three thousand words, the structure original research paper; sometime review paper should be as follows:

Papers: These are reports of significant research (typically less than 7000 words equivalent, including tables, figures, references), and comprise:

(a)Title should be relevant and commensurate with the theme of the paper.

(b) A brief Summary, "Abstract" (less than 150 words) containing the major results and conclusions.

(c) Up to ten keywords, that precisely identifies the paper's subject, purpose, and focus.

(d) An Introduction, giving necessary background excluding subheadings; objectives must be clearly declared.

(e) Resources and techniques with sufficient complete experimental details (wherever possible by reference) to permit repetition; sources of information must be given and numerical methods must be specified by reference, unless non-standard.

(f) Results should be presented concisely, by well-designed tables and/or figures; the same data may not be used in both; suitable statistical data should be given. All data must be obtained with attention to numerical detail in the planning stage. As reproduced design has been recognized to be important to experiments for a considerable time, the Editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned un-refereed;

(g) Discussion should cover the implications and consequences, not just recapitulating the results; conclusions should be summarizing.

(h) Brief Acknowledgements.

(i) References in the proper form.

Authors should very cautiously consider the preparation of papers to ensure that they communicate efficiently. Papers are much more likely to be accepted, if they are cautiously designed and laid out, contain few or no errors, are summarizing, and be conventional to the approach and instructions. They will in addition, be published with much less delays than those that require much technical and editorial correction.

The Editorial Board reserves the right to make literary corrections and to make suggestions to improve briefness.

It is vital, that authors take care in submitting a manuscript that is written in simple language and adheres to published guidelines.

Format

Language: The language of publication is UK English. Authors, for whom English is a second language, must have their manuscript efficiently edited by an English-speaking person before submission to make sure that, the English is of high excellence. It is preferable, that manuscripts should be professionally edited.

Standard Usage, Abbreviations, and Units: Spelling and hyphenation should be conventional to The Concise Oxford English Dictionary. Statistics and measurements should at all times be given in figures, e.g. 16 min, except for when the number begins a sentence. When the number does not refer to a unit of measurement it should be spelt in full unless, it is 160 or greater.

Abbreviations supposed to be used carefully. The abbreviated name or expression is supposed to be cited in full at first usage, followed by the conventional abbreviation in parentheses.

Metric SI units are supposed to generally be used excluding where they conflict with current practice or are confusing. For illustration, 1.4 l rather than 1.4 × 10-3 m3, or 4 mm somewhat than 4 × 10-3 m. Chemical formula and solutions must identify the form used, e.g. anhydrous or hydrated, and the concentration must be in clearly defined units. Common species names should be followed by underlines at the first mention. For following use the generic name should be constricted to a single letter, if it is clear.

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Abstract, used in Original Papers and Reviews:

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Many researchers searching for information online will use search engines such as Google, Yahoo or similar. By optimizing your paper for search engines, you will amplify the chance of someone finding it. This in turn will make it more likely to be viewed and/or cited in a further work. Global Journals Inc. (US) have compiled these guidelines to facilitate you to maximize the web-friendliness of the most public part of your paper.

Key Words

A major linchpin in research work for the writing research paper is the keyword search, which one will employ to find both library and Internet resources.

One must be persistent and creative in using keywords. An effective keyword search requires a strategy and planning a list of possible keywords and phrases to try.

Search engines for most searches, use Boolean searching, which is somewhat different from Internet searches. The Boolean search uses "operators," words (and, or, not, and near) that enable you to expand or narrow your affords. Tips for research paper while preparing research paper are very helpful guideline of research paper.

Choice of key words is first tool of tips to write research paper. Research paper writing is an art.A few tips for deciding as strategically as possible about keyword search:

- One should start brainstorming lists of possible keywords before even begin searching. Think about the most important concepts related to research work. Ask, "What words would a source have to include to be truly valuable in research paper?" Then consider synonyms for the important words.
- It may take the discovery of only one relevant paper to let steer in the right keyword direction because in most databases, the keywords under which a research paper is abstracted are listed with the paper.
- One should avoid outdated words.

Keywords are the key that opens a door to research work sources. Keyword searching is an art in which researcher's skills are bound to improve with experience and time.

Numerical Methods: Numerical methods used should be clear and, where appropriate, supported by references.

Acknowledgements: Please make these as concise as possible.

References

References follow the Harvard scheme of referencing. References in the text should cite the authors' names followed by the time of their publication, unless there are three or more authors when simply the first author's name is quoted followed by et al. unpublished work has to only be cited where necessary, and only in the text. Copies of references in press in other journals have to be supplied with submitted typescripts. It is necessary that all citations and references be carefully checked before submission, as mistakes or omissions will cause delays.

References to information on the World Wide Web can be given, but only if the information is available without charge to readers on an official site. Wikipedia and Similar websites are not allowed where anyone can change the information. Authors will be asked to make available electronic copies of the cited information for inclusion on the Global Journals Inc. (US) homepage at the judgment of the Editorial Board.

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For scanned images, the scanning resolution (at final image size) ought to be as follows to ensure good reproduction: line art: >650 dpi; halftones (including gel photographs) : >350 dpi; figures containing both halftone and line images: >650 dpi.

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TECHNIQUES FOR WRITING A GOOD QUALITY RESEARCH PAPER:

1. Choosing the topic: In most cases, the topic is searched by the interest of author but it can be also suggested by the guides. You can have several topics and then you can judge that in which topic or subject you are finding yourself most comfortable. This can be done by asking several questions to yourself, like Will I be able to carry our search in this area? Will I find all necessary recourses to accomplish the search? Will I be able to find all information in this field area? If the answer of these types of questions will be "Yes" then you can choose that topic. In most of the cases, you may have to conduct the surveys and have to visit several places because this field is related to Computer Science and Information Technology. Also, you may have to do a lot of work to find all rise and falls regarding the various data of that subject. Sometimes, detailed information plays a vital role, instead of short information.

2. Evaluators are human: First thing to remember that evaluators are also human being. They are not only meant for rejecting a paper. They are here to evaluate your paper. So, present your Best.

3. Think Like Evaluators: If you are in a confusion or getting demotivated that your paper will be accepted by evaluators or not, then think and try to evaluate your paper like an Evaluator. Try to understand that what an evaluator wants in your research paper and automatically you will have your answer.

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11. Revise what you wrote: When you write anything, always read it, summarize it and then finalize it.

12. Make all efforts: Make all efforts to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in introduction, that what is the need of a particular research paper. Polish your work by good skill of writing and always give an evaluator, what he wants.

13. Have backups: When you are going to do any important thing like making research paper, you should always have backup copies of it either in your computer or in paper. This will help you to not to lose any of your important.

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16. Use proper verb tense: Use proper verb tenses in your paper. Use past tense, to present those events that happened. Use present tense to indicate events that are going on. Use future tense to indicate future happening events. Use of improper and wrong tenses will confuse the evaluator. Avoid the sentences that are incomplete.

17. Never use online paper: If you are getting any paper on Internet, then never use it as your research paper because it might be possible that evaluator has already seen it or maybe it is outdated version.

18. Pick a good study spot: To do your research studies always try to pick a spot, which is quiet. Every spot is not for studies. Spot that suits you choose it and proceed further.

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20. Use good quality grammar: Always use a good quality grammar and use words that will throw positive impact on evaluator. Use of good quality grammar does not mean to use tough words, that for each word the evaluator has to go through dictionary. Do not start sentence with a conjunction. Do not fragment sentences. Eliminate one-word sentences. Ignore passive voice. Do not ever use a big word when a diminutive one would suffice. Verbs have to be in agreement with their subjects. Prepositions are not expressions to finish sentences with. It is incorrect to ever divide an infinitive. Avoid clichés like the disease. Also, always shun irritating alliteration. Use language that is simple and straight forward. put together a neat summary.

21. Arrangement of information: Each section of the main body should start with an opening sentence and there should be a changeover at the end of the section. Give only valid and powerful arguments to your topic. You may also maintain your arguments with records.

22. Never start in last minute: Always start at right time and give enough time to research work. Leaving everything to the last minute will degrade your paper and spoil your work.

23. Multitasking in research is not good: Doing several things at the same time proves bad habit in case of research activity. Research is an area, where everything has a particular time slot. Divide your research work in parts and do particular part in particular time slot.

24. Never copy others' work: Never copy others' work and give it your name because if evaluator has seen it anywhere you will be in trouble.

25. Take proper rest and food: No matter how many hours you spend for your research activity, if you are not taking care of your health then all your efforts will be in vain. For a quality research, study is must, and this can be done by taking proper rest and food.

26. Go for seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

27. Refresh your mind after intervals: Try to give rest to your mind by listening to soft music or by sleeping in intervals. This will also improve your memory.

28. Make colleagues: Always try to make colleagues. No matter how sharper or intelligent you are, if you make colleagues you can have several ideas, which will be helpful for your research.

29. Think technically: Always think technically. If anything happens, then search its reasons, its benefits, and demerits.

30. Think and then print: When you will go to print your paper, notice that tables are not be split, headings are not detached from their descriptions, and page sequence is maintained.

31. Adding unnecessary information: Do not add unnecessary information, like, I have used MS Excel to draw graph. Do not add irrelevant and inappropriate material. These all will create superfluous. Foreign terminology and phrases are not apropos. One should NEVER take a broad view. Analogy in script is like feathers on a snake. Not at all use a large word when a very small one would be sufficient. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Amplification is a billion times of inferior quality than sarcasm.

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33. Report concluded results: Use concluded results. From raw data, filter the results and then conclude your studies based on measurements and observations taken. Significant figures and appropriate number of decimal places should be used. Parenthetical remarks are prohibitive. Proofread carefully at final stage. In the end give outline to your arguments. Spot out perspectives of further study of this subject. Justify your conclusion by at the bottom of them with sufficient justifications and examples.

34. After conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print to the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects in your research.

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Key points to remember:

- Submit all work in its final form.
- Write your paper in the form, which is presented in the guidelines using the template.
- Please note the criterion for grading the final paper by peer-reviewers.

Final Points:

A purpose of organizing a research paper is to let people to interpret your effort selectively. The journal requires the following sections, submitted in the order listed, each section to start on a new page.

The introduction will be compiled from reference matter and will reflect the design processes or outline of basis that direct you to make study. As you will carry out the process of study, the method and process section will be constructed as like that. The result segment will show related statistics in nearly sequential order and will direct the reviewers next to the similar intellectual paths throughout the data that you took to carry out your study. The discussion section will provide understanding of the data and projections as to the implication of the results. The use of good quality references all through the paper will give the effort trustworthiness by representing an alertness of prior workings.

Writing a research paper is not an easy job no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record keeping are the only means to make straightforward the progression.

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To make a paper clear

· Adhere to recommended page limits

Mistakes to evade

- Insertion a title at the foot of a page with the subsequent text on the next page
- Separating a table/chart or figure - impound each figure/table to a single page
- Submitting a manuscript with pages out of sequence

In every sections of your document

· Use standard writing style including articles ("a", "the," etc.)

· Keep on paying attention on the research topic of the paper

· Use paragraphs to split each significant point (excluding for the abstract)

· Align the primary line of each section

· Present your points in sound order

· Use present tense to report well accepted

· Use past tense to describe specific results

· Shun familiar wording, don't address the reviewer directly, and don't use slang, slang language, or superlatives

· Shun use of extra pictures - include only those figures essential to presenting results

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Choose a revealing title. It should be short. It should not have non-standard acronyms or abbreviations. It should not exceed two printed lines. It should include the name(s) and address (es) of all authors.

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The summary should be two hundred words or less. It should briefly and clearly explain the key findings reported in the manuscript--must have precise statistics. It should not have abnormal acronyms or abbreviations. It should be logical in itself. Shun citing references at this point.

An abstract is a brief distinct paragraph summary of finished work or work in development. In a minute or less a reviewer can be taught the foundation behind the study, common approach to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Yet, use comprehensive sentences and do not let go readability for briefness. You can maintain it succinct by phrasing sentences so that they provide more than lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study, with the subsequent elements in any summary. Try to maintain the initial two items to no more than one ruling each.

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- Fundamental goal
- To the point depiction of the research
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- Significant conclusions or questions that track from the research(es)

Approach:

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- Center on shortening results - bound background information to a verdict or two, if completely necessary
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The **Introduction** should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable to comprehend and calculate the purpose of your study without having to submit to other works. The basis for the study should be offered. Give most important references but shun difficult to make a comprehensive appraisal of the topic. In the introduction, describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will have no attention in your result. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here. Following approach can create a valuable beginning:

- Explain the value (significance) of the study
- Shield the model - why did you employ this particular system or method? What is its compensation? You strength remark on its appropriateness from a abstract point of vision as well as point out sensible reasons for using it.
- Present a justification. Status your particular theory (es) or aim(s), and describe the logic that led you to choose them.
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Approach:

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Materials:

- Explain materials individually only if the study is so complex that it saves liberty this way.
- Embrace particular materials, and any tools or provisions that are not frequently found in laboratories.
- Do not take in frequently found.
- If use of a definite type of tools.
- Materials may be reported in a part section or else they may be recognized along with your measures.

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- Report the method (not particulars of each process that engaged the same methodology)
- Describe the method entirely
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures
- Simplify - details how procedures were completed not how they were exclusively performed on a particular day.
- If well known procedures were used, account the procedure by name, possibly with reference, and that's all.

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- It is embarrassed or not possible to use vigorous voice when documenting methods with no using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result when script up the methods most authors use third person passive voice.
- Use standard style in this and in every other part of the paper - avoid familiar lists, and use full sentences.

What to keep away from

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings - save it for the argument.
- Leave out information that is immaterial to a third party.

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The principle of a results segment is to present and demonstrate your conclusion. Create this part a entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Carry on to be to the point, by means of statistics and tables, if suitable, to present consequences most efficiently.You must obviously differentiate material that would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matter should not be submitted at all except requested by the instructor.

Content

- Sum up your conclusion in text and demonstrate them, if suitable, with figures and tables.
- In manuscript, explain each of your consequences, point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation an exacting study.
- Explain results of control experiments and comprise remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or in manuscript form.

What to stay away from

- Do not discuss or infer your outcome, report surroundings information, or try to explain anything.
- Not at all, take in raw data or intermediate calculations in a research manuscript.
- Do not present the similar data more than once.
- Manuscript should complement any figures or tables, not duplicate the identical information.
- Never confuse figures with tables - there is a difference.

Approach

- As forever, use past tense when you submit to your results, and put the whole thing in a reasonable order.
- Put figures and tables, appropriately numbered, in order at the end of the report
- If you desire, you may place your figures and tables properly within the text of your results part.

Figures and tables

- If you put figures and tables at the end of the details, make certain that they are visibly distinguished from any attach appendix materials, such as raw facts
- Despite of position, each figure must be numbered one after the other and complete with subtitle
- In spite of position, each table must be titled, numbered one after the other and complete with heading
- All figure and table must be adequately complete that it could situate on its own, divide from text

Discussion:

The Discussion is expected the trickiest segment to write and describe. A lot of papers submitted for journal are discarded based on problems with the Discussion. There is no head of state for how long a argument should be. Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implication of the study. The purpose here is to offer an understanding of your results and hold up for all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of result should be visibly described. Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved with prospect, and let it drop at that.

- Make a decision if each premise is supported, discarded, or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."
- Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work
- You may propose future guidelines, such as how the experiment might be personalized to accomplish a new idea.
- Give details all of your remarks as much as possible, focus on mechanisms.
- Make a decision if the tentative design sufficiently addressed the theory, and whether or not it was correctly restricted.
- Try to present substitute explanations if sensible alternatives be present.
- One research will not counter an overall question, so maintain the large picture in mind, where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

- When you refer to information, differentiate data generated by your own studies from available information
- Submit to work done by specific persons (including you) in past tense.
- Submit to generally acknowledged facts and main beliefs in present tense.

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Methods and Procedures	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
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Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

INDEX

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ISSN 9755896