Original Article

Studies of left ventricular functions by systolic time intervals on exposure to dry immersion

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ABSTRACT

Eleven healthy subjects were assessed for cardiovascular responses on simulated hypogravic exposure by the method of 4 hrs of Dry Immersion (DI). Various parameters measured were Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Pulse Pressure (PP), Mean Arterial Pressure (MAP), Total Peripheral Resistance (TPR). Systolic Time Intervals (STI) i.e., Total Electromechanical Systole (QS_2), Left Ventricular Ejection Time (LVET), Pre Ejection Period (PEP) and PEP/ LVET ratio were utilized for non invasive assessment of left ventricular function. Immediately on induction to DI from quiet standing there was significant decrease in HR, SBP, DBP, MAP, PP, TPR, PEP and PEP/LVET ratio and increase in QS_2 and LVET. During the course of DI, PEP showed an increase and HR showed a decrease from its respective zero min DI values. LVET and QS_2 showed gradual increase till 2 hrs of DI followed by decrease till the end of 4 hrs of DI. PEP/LVET ratio was decreased initially followed by gradual increase till the end of DI. Blood pressure showed gradual decrease during the course of DI. Changes in STI parameters were found sensitive indicators of left ventricular function changes due to cephalic fluid shift and consequent relative diuresis as seen in this study. Comparison between 5 min quiet standing conducted before and after the DI revealed significantly higher PEP and PEP/LVET ratio with decreased stroke volume and cardiac output during post exposure quiet standing, while routine cardiovascular parameters showed no significant differences. Left ventricular functions appear to be affected earlier than the routine orthostatic cardiovascular functions following exposure to simulated weightlessness.

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The physiological changes on exposure to microgravity were seen to be an adaptive response of the body [1,2,3]. Study of these physiological changes in actual space flight is difficult; hence, to gain an insight, a variety of ground-based studies using analogues of weightlessness have been developed [1,4,5]. Water immersion has been used as an analogue for microgravity by a number of investigators [6,7]. To avoid the problems of wet immersion, Sulhenko in 1976 had employed a dry immersion technique in which subjects are protected from water contact by a thin plastic sheet [4]. This is probably the ideal analogue of weightlessness as it overcomes the problems of skin maceration, maintenance of hygiene and discomfort of head down tilt.

The physiological response in hypogravic condition in cephalic fluid shift, which causes an increase in central circulation parameters including central venous pressure (CVP) and central blood volume (CBV), which in turn activates various compensatory mechanisms to reduce extracellular fluid volume [2,3,7,8].

The adaptation is achieved primarily by diuresis and reduction in plasma volume associated with a

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decrease in antidiuretic hormone, aldosterone, renin-angiotension activity and a reduction in sympathetic nervous system stimulation [3, 6, 7, 9]. The changes in cardiovascular dynamics due to fluid shift and the adaptive reflex responses lead to alterations in left ventricular functions. This was studied by STI measurements by non-invasive methods as an appropriate index of cardiovascular deconditioning [10, 11] and consists of the following:

QS_2. This period is measured from onset of Q wave in electrocardiograph (ECG) to the first high frequency aortic component of the second heart sound. It includes electromechanical lag (EML), isovolumetric contraction time (IVCT), PEP and LVET. It is primarily used to measure PEP when the LVET values are known.

PEP (QS_2 - LVET). Extends from depolarization of LV to the start of ejection and includes the time for depolarization. It is closely related to the haemodynamic status of the heart and is a better measure of the contractility of the heart. Normal values range from 80 to 105 milli seconds (mean 100 $\pm$ 13 milli seconds).

LVET. It is the time interval from the upstroke of the carotid pulse wave (indicates rise in aortic pressure) to its incisura (indicates aortic valve closure). It represents the isotonic phase of left ventricular systole and is inversely related to heart rate. It has high correlation with stroke volume (SV) and cardiac output (CO) and is inversely related to rate of left ventricular ejection. Decrease in SV shortens LVET. QS_2 and LVET have an inverse but linear relationship with heart rate, whereas PEP is affected only slightly.

PEP/LVET ratio. Most of the individual STI's are influenced by factors like HR, SV, CO, sex, age, physical condition and other factors. Hence, attempt has been made to derive a sensitive index having high correlation with corresponding haemodynamic indices and direct measurement of contractility. It uses uncorrected values of PEP and LVET. The normal values being 0.345 $\pm$ 0.036 increasing to almost 0.6 in patients with heart failure. This ratio is maximum in patients with heart failure and is the most reliable and sensitive index of cardiac performance [12].

STI from Apollo - 17 crewmen remained elevated longer post flight than the response criteria of HR, BP and percent changes in leg volume, all of which returned to preflight levels by the second day post-flight. STI changes in post-flight Skylab 3 and 4 crewmen were back within pre-flight values by 2-4 weeks [13].

In a study at the Institute of Aerospace Medicine (IAM), short duration hypogravic exposure of 2 hrs (DI) was found to increase the PEP during post exposure Head Up Tilt (HUT) and this was suggested as an early indication of indication of CVS deconditioning [14]. Two other studies consisting of 6 and 12 hours of DI also showed significant cardio vascular system (CVS) deconditioning on post exposure HUT, which was evidenced by marked fall in orthostatic tolerance after 6 hrs of DI and increased intolerance on 12 hrs of DI [15, 16].

The present study aimed to find out the details of the changes in LV functions as measured by STI within the first 4 hours of exposure to hypogravity simulation by the method of DI. It also aimed to see the extent and nature of cardiovascular deconditioning taking place if any, before the overt symptoms of deconditioning appeared.

Material and Methods

Eleven healthy adult male volunteers with a mean age of 28 $\pm$ 3 years, height of 170 $\pm$ 7 cms and weight of 63 $\pm$ 9 kg participated in this study. Details of the study were explained and informed consent was obtained from them. Dry immersion facility at IAM was used. Three channels Nihon-Kohden Cardioflax recorder with facilities of simultaneous recording of ECG, Phonocardiogram (PCG) and Indirect Carotid Arterial Pulse Tracing (CAP) and sphygmomanometer was used.

Experimental protocol followed was such that subjects reported at a fixed time of the day. Control reading of STI and BP was taken in supine position followed by immediately on standing and then at the end of quiet standing. Recordings of STI and BP were made at 0 min, 5 min, 15 min, 1 hr, 1½ hr, 2 ½ hrs and 4 hrs of dry floatation. Pre and post exposure venous blood samples were taken during supine position at 9 min and at the end of the floatation to see the change in plasma volume, if any. Post exposure STI and BP recording were taken on coming out of DI in supine position, immediately on standing and after 5 min of quiet standing. Fluid / food intake and output were noted during the course of the experiment to find out the loss in total body mass.

STI's were measured through five consecutive cycles in each set of recording to the nearest 0.5 mm (5 msec) and averaging was done. The various time intervals, which were measured, have already been mentioned. Heart rate corrected indices of systolic time intervals; QS2-I, LVET-I and PEP-I were calculated by Weissler's formula.

- QS2-I = QS2 + 2.1 x HR
- LVET-I = LVET + 1.7 x HR
- PEP-I = PEP + 0.4 x HR

Stroke volume was calculated indirectly by Harvey's equation. Cardiac output was calculated from SV x HR. Total peripheral resistance was calculated by dividing MAP by CO. Haemoglobin and haematocrit were calculated by cyanmethaemoglobin and Wintrobe's method respectively. Plasma volume change was calculated by using Harrison's formula [9100 x Hb1 / Hb2) x (100 - Hct2/100 - Hct) - 100].

Statistical analysis was done by taking eleven subject's data on heart rate, BP, STI parameters, SV, CO and TPR at different time intervals during the test protocol and on Hb, Hct at pre and post DI exposure for mean values with standard deviation (SD). Comparison of the the cardiovascular parameters on DI at different time intervals and between pre and post exposure supine and quiet standing were made by using Students paired 't' test [17]. 'p' values were read from 't' values and a 'p' of 0.05 and less was considered as significant.

Results

Table - 1 shows physical characteristics of the subjects. Table - 2 presents values of HR, SBP, DBP, PP and MAP before, during and after 4 hrs of DI. Table - 3 shows mean ± SD of QS_2, QS_2-1, LVET, LVET-1, PEP, PEP-1 and PEP/ LVET ratio at different time intervals during the test protocol. Table - 4 shows mean ± SD values of SV, Stroke index (SI), CO, cardiac index (CI) and total peripheral resistance(TPR) at different time intervals during the test protocol. Table - 5 shows individual values with mean ± SD of haematological data before and after DI. Individual fluid balance data during 4 hrs of DI as measured from body weight changes, fluid intake and output measures are presented in Table - 6. Results summary is as follows:

Immediately on induction of DI from standing posture HR, SBP, pulse pressure (PP), MAP, PEP, PEP / LVET ratio and TPR showed immediate significant decrease in comparison to 5 min standing values. QS_2, LVET, CO, CI, SV and SI showed significant increase in comparison to 5 min standing value. After immediate changes, during the course of 4 hrs of DI, two distinct phases of changes noted in respect of most of the cardiovascular parameters were as follows:

(a) **First 2 hrs of DI.** HR showed a marginal rise till 15 mins followed by decline till 2 hrs of DI. SBP, DBP, MAP and PP showed further decrease. QS_2 and LVET showed further increase and reached their maximum vaues at 1½ hrs and 2 hrs respectively. PEP and PEP/LVET ratio showed gradual increase after initial fall. SV showed further increase and reached its maximum value at 2 hrs, whereas, CO reached its maximum at 30 minutes and subsequently showed a gradual decrease.

Table-1
Physical characteristics of the subjects (n = 11)

Serial No.	Subject	Age (Yr)	Height (Cm)	Weight (Kg)	BSA (Sqm)
1	PG	26	179.5	63	1.79
2	AR	30	177	70	1.85
3	AA	26	177	82	1.99
4	SD	22	173	58	1.67
5	PB	28	166	64	1.70
6	SM	30	174	63	1.75
7	SR	26	169	68	1.77
8	BB	30	161	49	1.48
9	GG	23	167	62	1.69
10	SD	34	156	58	1.55
11	SS	28	167	53	1.57
Mean		27.54	169.68	62.72	1.71
SD		± 3.43	± 7.23	± 8.84	± 0.14
Range		22-34	156-179.5	49-82	1.48-1.99

(b) **Subsequent 2 hrs.** HR showed marginal rise after 2 hrs but remained below 0 min value. SBP, DBP, PP and MAP remained decreased in comparison to 0 min DI value. QS_2 and LVET showed gradual decrease from 1½ hrs and 2 hrs onwards respectively till 4 hrs of DI. PEP and PEP/LVET ratio increased gradually and from 3 hrs onwards it became significantly higher in comparison to 0 min DI value. SV showed gradual reduction since 2 hrs of DI that continued till 4 hrs of DI. CO reduced gradually from 30 min onwards and remained below 0 min DI value thereafter.

(c) Comparison between pre and post exposure supine and 5 min standing values of HR, BP and QS_2 showed no significant differences. LVET showed significant reduction in post exposure supine value. PEP and PEP/LVET ratio showed significant increase in post exposure supine and 5 min standing values. SV and CO showed significant decreases in post exposure supine and 5 min standing values. There was significant reduction in plasma volume and loss in body mass noted at the end of 4 hrs of DI.

Discussion

Inflight changes in cardiovascular parameters that takes place during actual space flight is the immediate shift of intravascular fluid from the lower part of the body to the thorax and upper parts [2, 6,18]. There is reduction in calf girth [4], negative water balance caused by natriuresis and diuresis leading to hypohydration. During space flight, HR decreases in flight in the initial few days followed by a slight rise [1,5]. There is increase in CVP, CO and SV initially [19]. There is a variable change in SBP and PP; DBP showed drop in most of the studies [1, 20, 21]. STI during space flight by Vorobyov et al [21] using kinetocardiography showed significant reduction of IVCT and IVRT and unstable rise of ejection (LVET) and fast filling phase. Nicogossian et al [22] and other researchers [23] have also reported the same change. The post flight STI data at rest and during lower body negative pressure also suggests a decrease in pre-load and decreased myocardial contractility [24, 25]. Preflight and postflight Bio-stereo-metric analysis of body form on the nine Skylab astronauts, revealed a loss of volume and mass of the body of the order of 2.66 ± 1.83 lit and 3.03 ± 1.64 kg respectively [13].

Major cardiovascular changes noted during the present study of 4 hrs of DI were as follows:

(a) **HR.** It showed immediate fall on immersion as compared to 5 min standing value followed by further significant fall till 2 hrs and finally a marginal rise but still below the 0 min DI value. Studies by different authors [18, 19, 20] found the same trend. Blomqvist et al [19] found an increase in CVP by 1.9 cm of water on immersion at 30 min that came down below base level by 90 min. This initial increase in CVP and the consequent stretch of right atrial receptors, reflexly lower the HR through the baroreceptors.

Table - 2
HR and BP responses before, during and after DI
(Mean ± SD)

Time (min)	HR (bpm)	SBP (mm Hg)	DBP (mm Hg)	PP (mm Hg)	MAP (mm Hg)
Pre exposure					
0 min supine	69 ± 10	115 ± 7	69 ± 11	46 ± 12	84 ± 9
0 min standing	82 ± 13	111 ± 10	76 ± 10	35 ± 0.4	88 ± 10
5 min standing	85 ± 12	113 ± 9	77 ± 11	36 ± 9	89 ± 9
Dry Immersion					
0 min	68 ± 10	110 ± 7	67 ± 9	43 ± 8	81 ± 8
5 min	68 ± 9	107 ± 6	65 ± 9	42 ± 7	79 ± 7
15 min	69 ± 9	106 ± 4	62 ± 8	44 ± 7	77 ± 5
30 min	66 ± 9	108 ± 7	63 ± 8	45 ± 7	78 ± 7
60 min	64 ± 9	106 ± 8	66 ± 10	40 ± 6	79 ± 9
90 min	63 ± 8	107 ± 8	65 ± 9	42 ± 8	98 ± 7
120 min	62 ± 8	108 ± 7	66 ± 9	42 ± 6	80 ± 7
150 min	64 ± 10	109 ± 6	63 ± 7	46 ± 7	78 ± 6
180 min	63 ± 8	110 ± 8	64 ± 9	46 ± 6	79 ± 8
210 min	63 ± 9	109 ± 9	65 ± 6	44 ± 8	80 ± 6
240 min	64 ± 9	108 ± 8	65 ± 8	43 ± 6	79 ± 8
Post exposure					
0 min supine	67 ± 12	112 ± 8	74 ± 8	38 ± 6	87 ± 6
0 min standing	85 ± 12	110 ± 10	78 ± 10	32 ± 10	89 ± 8
5 min standing	83 ± 12	111 ± 9	80 ± 9	31 ± 9	90 ± 8

(b) **BP**. In the present study, there was significant reductions in DBP and MAP and a marginal drop in SBP and PP during the course of 4 hrs of DI. Short term immersion experiments showed a decrease of arterial BP in the first 2 hrs followed by marginal increase till 4 hrs of immersion [5]. Similar findings have been found in other studies [16, 19].

(c) **SV and CO** . There was an immediate increase on DI and thereafter it increased gradually and attained its maximum value at 2 hrs of DI followed by gradual reduction till 4 hrs. Other studies reported similar findings [19, 26]. Arbovelius et al [18] reported an initial shift of 700 ml of blood to the central circulation leading to increase in stroke volume by 35% and CO by 32% on water immersion.

(d) **PV.** The present study showed a definite reduction in plasma volume after 4 hrs of DI in all the cases except one, which showed no change. It varied from 0-14.5% with a mean value of 4.8%. The study also showed a loss in total body mass at the end of 4 hrs of DI of the order of 0.05 - 1.8% with a mean value of 0.68%. Other studies showed similar changes [1, 6, 19, 27, 28, 29].

Table - 3
STI values and their HR corrected indices with PEP/LVET ratio before, during and after DI

Time (min)	QS2 (ms)	QS2(1) (ms)	LVET (ms)	LVET(1) (ms)	PEP (ms)	PEP(I) (ms)	PEP/LVET
Pre exposure							
0 min supine	382 ± 19	527 ± 13	283 ± 17	400 ± 10	99 ± 9	127 ± 10	0.349 ± 0.04
0 min standing	334 ± 25	507 ± 11	231 ± 21	372 ± 11	103 ± 13	135 ± 12	0.445 ± 0.06
5 min standing	341 ± 19	520 ± 18	227 ± 18	372 ± 15	114 ± 15	148 ± 15	0.502 ± 0.08
Dry immersion							
0 min	380 ± 19	522 ± 13	286 ± 17	401 ± 11	95 ± 13	121 ± 13	0.328 ± 0.05
5 min	381 ± 15	526 ± 13	288 ± 15	400 ± 14	93 ± 13	126 ± 9	0.322 ± 0.03
15 min	387 ± 16	533 ± 12	289 ± 15	402 ± 19	98 ± 10	131 ± 10	0.339 ± 0.04
30 min	390 ± 16	531 ± 13	296 ± 12	409 ± 9	94 ± 12	122 ± 13	0.317 ± 0.04
60 min	395 ± 15	530 ± 14	299 ± 1	403 ± 16	96 ± 11	127 ± 20	0.32 ± 0.04
90 min	402 ± 14	534 ± 14	300 ± 12	406 ± 10	102 ± 1	128 ± 13	0.340 ± 0.04
120 min	401 ± 15	532 ± 11	301 ± 14	407 ± 10	100 ± 13	125 ± 13	0.332 ± 0.05
150 min	397 ± 18	530 ± 17	296 ± 14	404 ± 8	101 ± 14	126 ± 12	0.341 ± 0.03
180 min	392 ± 12	529 ± 12	292 ± 18	404 ± 11	100 ± 10	125 ± 10	0.342 ± 0.05
210 min	293 ± 30	526 ± 11	289 ± 18	396 ± 8	104 ± 8	130 ± 10	0.359 ± 0.04
240 min	394 ± 12	528 ± 7	289 ± 16	396 ± 10	105 ± 5	132 ± 8	0.363 ± 0.03
Post exposure							
0 min supine	383 ± 19	523 ± 11	270 ± 25	384 ± 8	113 ± 12	139 ± 14	0.418 ± 0.03
0 min standing	331 ± 22	505 ± 34	221 ± 14	326 ± 18	110 ± 18	143 ± 21	0.497 ± 0.04
5 min standing	338 ± 23	512 ± 8	220 ± 19	361 ± 10	118 ± 12	151 ± 10	0.536 ± 0.05

(e) **STI** measured in this study shows the following changes:

(f) **QS_2 and LVET.** They showed significant increase immediately on DI as compared to pre-exposure 5 min standing value. Thereafter, QS_2 showed further increase and reached its highest value at 1½ hrs and reduced gradually throughout DI but still remained above the 0 min DI value. LVET also showed further increase but reached its highest value at 2 hrs of DI followed by gradual decrease till end of DI but remained above the 0 min DI value.

(g) **PEP and PEP/LVET ratio.** These showed significant reduction immediately on DI as compared to pre-exposure 5 min standing value. Thereafter, PEP and PEP/LVET ratio both showed gradual increase throughout the DI and became significantly increased from 3 hrs onwards and the increase continued till 4 hr of DI as compared to 0 min DI value. Study by Frey et at [8] in STI changes in leg elevation of 40 sec duration showed an immediate increase in LVET, which is more after 6 sec of elevation and remained elevated till 40 secs indicating an increase in stroke volume. PEP and PEP/LVET ratio, which are inversely correlated with ejection fraction and are also a measure of ventricular performance, were significantly reduced during the leg up period. Other studies showed similar responses [14].

Table - 4

Responses of haemodynamic parameters before, during and after DI (Mean ± SD)

Time (min)	SV (ml)	SI (ml/sqm)	CO (L/min)	CI (L/min/m2)	TPR (mmHg/L/min)
Pre exposure					
0 min supine	84 ± 8	49 ± 6	5.7 ± 0.58	3.38 ± 0.46	15 ± 2
0 min standing	59 ± 9	36 ± 7	4.77 ± 0.48	2.84 ± 0.42	18 ± 2
5 min standing	58 ± 8	35 ± 7	4.87 ± 0.57	2.87 ± 0.52	18 ± 3
Dry Immersion					
0 min	85 ± 7	50 ± 6	5.7 ± 0.67	3.36 ± 0.53	14 ± 2
5 min	86 ± 7	51 ± 6	5.79 ± 0.62	3.42 ± 0.54	14 ± 2
15 min	87 ± 7	51 ± 6	5.98 ± 0.64	3.52 ± 0.55	13 ± 2
30 min	90 ± 5	53 ± 5	5.96 ± 0.63	5.57 ± 0.40	13 ± 2
60 min	90 ± 6	53 ± 6	5.78 ± 0.64	3.44 ± 0.48	14 ± 2
90 min	91 ± 5	54 ± 6	5.70 ± 0.60	3.33 ± 0.45	14 ± 1
120 min	92 ± 6	54 ± 5	5.68 ± 0.55	3.34 ± 0.41	14 ± 2
150 min	89 ± 6	53 ± 6	5.66 ± 0.64	3.32 ± 0.43	14 ± 1
180 min	88 ± 8	52 ± 7	5.72 ± 0.49	3.37 ± 0.49	14 ± 1
210 min	86 ± 8	51 ± 7	5.35 ± 0.49	3.15 ± 0.42	15 ± 2
240 min	86 ± 7	51 ± 7	5.40 ± 0.41	3.20 ± 0.37	15 ± 2
Post exposure					
0 min supine	77 ± 11	45 ± 8	5.03 ± 0.35	2.96 ± 0.34	17 ± 2
0 min standing	54 ± 6	32 ± 6	4.49 ± 0.63	2.86 ± 0.59	21 ± 4
5 min standing	53 ± 7	32 ± 7	4.35 ± 0.41	2.56 ± 0.28	21 ± 2

Table - 5

Hb and Hct responses before and after 4 hrs of DI Mean ± SD (n=11)

No. of Subjects	Pre and post expo Hb1 (mg%)	Hb2 (mg%)	Pre and post expo Hct1 (%)	Hct2 (%)
1.	17.88	17.99	49	49
2.	15.91	16.69	43	44
3.	18.33	19.55	48	48.5
4.	15.81	16.23	45	45
5.	14.89	15.19	42	42.5
6.	15.98	17.57	52	54
7.	12.85	12.75	47	47.5
8.	11.59	11.56	46	46
9.	13.43	14.82	45	45
10.	13.77	14.28	50	50
11.	14.7	15.25	45	45.5
Mean	15.01	15.62	46.54	47
SD	± 2.05	± 2.32	± 3.01	± 3.24

Table - 6

Percentage of plasma volume, body mass loss and total urine output at the end of 4 hrs of DI (n=11)

No. of Subjects	Plasma vol loss (%)	body mass loss (%)	Urine output (ml)
1.	-1	-0.36	570
2.	-7.85	-1.0	750
3.	-7	-0.27	1180
4.	-3	-1.8	970
5.	-3.08	-0.65	600
6.	-14.5	-1.41	950
7.	-0.31	-0.49	1075
8.	0	-0.46	1000
9.	-9.4	-0.05	600
10.	-3.6	-0.66	1190
11.	-3.14	-0.37	370
Mean	-4.80	-0.68	841.36
SD	± 4.44	± 0.52	± 276.58

The results can be explained by the fact that due to initial increase in pre-load and carotid baroreceptor activation there was increase in LVET initially and decrease in PEP and PEP/ LVET ratio. Increased preload produces Frank-Starling effect and reduces PEP; initial increase in LVET can be explained by a decrease in after load and increase in preload. Subsequently, after 2 hrs decrease in LVET can be taken as an indication of reflex sympathetic adaptation on cardiac ionotropy. Increase in PEP/LVET ratio after 2 hrs can be explained on the same basis i.e., decrease in after load because of DI induced relative diuresis, decrease in plasma volume and decrease in myocardial ionotropism.

Comparison of routine cardiovascular parameters like HR and BP on 5 min quiet standing pre and post exposure revealed no significant differences, thus indicating no gross change in orthostatic tolerance by means of 4 hrs of exposure to hypogravic simulation. Nevertheless, the adaptive changes were manifest in the form of decreased left ventricular functions as evaluated by STI.

These observations emphasize on the significance of left ventricular functions as early indicators of cardiovascular changes on exposure to hypogravic environment and reiterates the suggestion of Bergman et al [30] for use of STI in the assessment of cardiovascular deconditioning following exposure to weightlessness.

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